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LUMBAR AND SACRAL COMPRESSION RADICULITIS (HERNIATED LUMBAR DISK SYNDROME)*

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THIS paper is a report of a study of certain back injuries having to do with ruptured intervertebral disks, as well as the compressive radiculitis in the same area, that were admitted to the neurosurgical service of the Boston City Hospital during the seventeen years between 1937 and 1955. It is a summary of the clinical aspects of the problems and neither includes any patients with bony vertebral injuries nor any follow-up except immediate postoperative or post-hospitalization end results. Long-term end results will be reported in another communication.

MATERIAL

The total number of patients involved was 545. Their ages ranged from a high of sixty-eight to a low of fifteen years. There were 402 men and 143 women. There were 124 patients with multiple (2 or more) admissions. The greatest number of admissions per patient was 14.

Three hundred and fifty-six patients were operated upon 375 times, and the diagnosis verified in all these cases by actual visualization of the pathology in the operative field. Of these, 95 were patients with multiple admissions. Another 189 were not operated upon. The diagnosis in these latter cases was made on the basis of clinical examination or myelogram or both. There were 29 patients who had multiple admissions in this latter group.

CAUSE OF INJURY

The possible causes of the injuries resulting in a compressive lumbar radiculitis and commonly associated with ruptured lumbar or lumbosacral disks are legion. They range from no known cause through athletics and including jujitsu and post-partum back strain, to getting into or out of bed. The commonest single cause was lifting. This was assigned 167 times, 101 of which had the diagnosis verified. The next most frequent cause was a fall, 47 of which occurred among the operated and 52 among the nonoperated cases. The only other numerically significant causes were "no cause" operated — 57, nonoperated — 20; struck on back or leg — 11 and 9 times respectively; stooping — 12 and 7 times; automobile accident — 9 each; slipping — 11 and 3 times; athletics — 13 and 3; and the scar of a previous back operation — 11 and 2. Various other causes, which only occurred 10 or fewer times, were as follows: strained back; post partum; pulling or pushing; standing or walking; coming erect from a sitting or lying position; working in a cramped position; exposure; coughing; strenuous work; psychosis; back snap; prolonged suspension by 1 arm; crush; frostbite; following an infection; driving automobile; exercise; housework; reaching; postspinal anesthesia; and cause doubtful.

It is apparent from this analysis that while almost any bodily activity *can* produce back alterations that lead to compressive radiculitis the commonest causes and therefore the ones that should raise a suspicion of such an injury in the surgeon's mind are lifting, a fall and "no cause."

THE CASUAL BACKGROUND

In analyzing these 545 cases from this point of view it was obvious that such analysis would be futile, erroneous and confusing unless the first historical evidence of a back injury was chosen as the activating or trigger force that produced the underlying changes that manifested themselves and grew worse as time progressed. This view was supported by the now well accepted theory that while it is certainly possible, as the result of any single application of force applied to a given vertebra at a proper angle or impact, to rupture the posterior spinal ligament and the annulus

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All statistical figures, as well as other opinions, deductions, conclusions and similar data, are derived from or are the outgrowth of the experiences drawn from this particular series of cases alone.

Later on, other papers will be written on such subjects as long-term follow-up studies, the surgical pathology of the removed disk tissue and the intervertebral-facet problem among others, in which comparisons will be made between the facts deduced from this series of cases and various series published by other authors interested in this confusing problem.

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and thus permit the contained nucleus to emerge and exert disabling pressure on any given spinal root or on the cauda, this is not the usual mechanism. This latter is commonly a succession of minor back injuries that increase the root irritation and the associated compression as time passes, with resultant increase in symptomatology. This depends for effectiveness on the degree of damage done originally to the posterior spinal ligament and annulus as well as on their resultant future capacity to withstand further repeated insults. The evidence, in addition to being historical, depended on the patients' statements as well as the

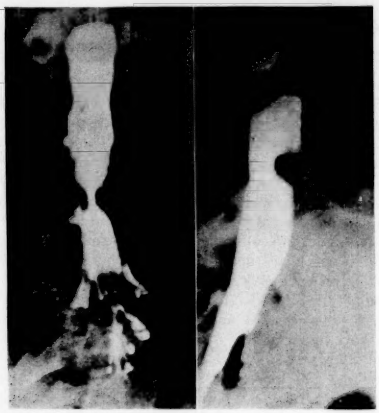

FIGURE 1. *Lipiodol Myelogram — Positive Anteroposterior and Oblique Views (Courtesy of Dr. Walter Wegner).*

significant number of multiple admissions referred to above and the small number of patients (4) admitted during the first week after their injury.

INDUSTRIAL VS. NONINDUSTRIAL CASES

It was found in the 545 cases studied herewith that 341 were industrial and the remainder (204) were nonindustrial. Forty-two per cent, or 145 of the 341 industrial cases, were hospitalized during the first year after injury as were 41 per cent of the 204 nonindustrial cases. During the two years after injury 67 per cent of industrial and 61 per cent of nonindustrial cases had been hospitalized by us. Twenty years after injury 98 per cent of the industrial and 93 per cent of the nonindustrial cases had been hospitalized. Three industrial and 1 nonindustrial case were seen in the hospital within four days of injury, 2 being seen within twenty-four hours. There was 1 industrial case that came for treatment fifty-three years, and 1 many years after injury, and 1 in which the time elapsed between injury and hospitalization could not be determined.

It is apparent that in this series the time interval between the patient's injury and his hospitalization for investigation or operation was the same whether the original accident was industrial or nonindustrial. Two thirds of the industrial and slightly less than two thirds of the non-industrial cases were hospitalized during their first two years after injury. Grouped with the industrial cases were the injuries sustained as the result of automobile accidents.

MYELOGRAMS

It is well recognized that one of the most helpful diagnostic procedures in patients with a root or the cauda equina compressed by a protruded or extruded nucleus pulposus is a myelogram. It is also well recognized that a significant percentage of error accompanies this procedure. An attempt has been made over these past seventeen years, first, to determine the most practical radiopaque medium to use, secondly, to learn, if possible, the probable error involved in its use and thirdly, to evaluate the complications arising from the use of the various mediums. In connection with this study I have found it extremely valuable to be able to read the films myself and thus to correlate the preoperative myelographic diagnosis with the condition actually found at operation.

In the earliest patients lipiodol was used for this purpose. Twenty-five lipiodol myelograms were performed, 17 on patients in whom the myelographic diagnosis was checked against the operative findings and 6 on patients that were not operated upon. In these latter, therefore, verification or denial of the myelographic diagnosis was not possible. In this, as in all the succeeding paragraphs of this section, agreement between the preoperative myelographic diagnosis and the pathology found at operation was expressed as positive, nonagreement as negative, and an unreadable or technically poor myelogram as unsatisfactory. Of the 17 verified lipiodol myelograms 9 were positive (Fig. 1), 4 were negative, and 4 were unsatisfactory. The respective percentages were 53, 24 and 24. Postlipiodol myelographic complications occurred in 2, or 8 per cent, of the 25 myelograms performed.

Air or oxygen were the next mediums that were used. Eighty-seven air or oxygen myelograms were performed by both single and two-needle technic[1] on 76 patients. Thirty-four (40 per cent) were positive (Fig. 2), 16 (18 per cent) were negative, and 8 (9 per cent) were unsatisfactory. Three patients (3 per cent) had postmyelogram complications — all headaches.

It was obvious that 47 per cent erroneous or unreadable lipiodol films was an undesirable high number and that a similar 27 per cent of the air myelograms was equally so.

In an attempt to find a more visually accurate medium the water-soluble radiopaque medium Skiodan was used. This gave a very much more readable film

— one that actually outlined the root filaments (Fig. 3). One hundred and twenty-five of these myelograms were performed on 97 patients. Eighty-eight (70 per cent) were verified by operation. Ten (10 per cent) proved at operation to be wrong, and 15 (17 per cent) proved to be unsatisfactory. While the grams). Thus, the incidence of correct preoperative diagnosis was distinctly greater than that with lipiodol and air but less than that with Skiodan (54 compared with 50, 40 and 70 per cent), the percentage of error also compared favorably with the others (13 compared with 25, 18 and 11 per cent), and the inci-

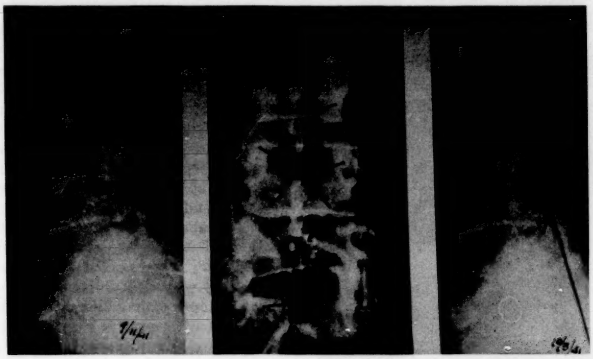

FIGURE 2. *Oxygen Myelogram — Positive Anteroposterior, Lateral and Oblique Views.*

28 per cent error traceable to wrong or impossible interpretation of the films, although still too high, was sufficiently low to justify the continued use of Skiodan in preference to either lipiodol, air or oxygen if there were no other objections, it was unfortunately true that the postmyelographic complications of this dye were of such severity and number as to render this medium unsuitable for further use in this field. The 125 myelograms were accompanied by 23 severe complications (18 per cent). These included, among other less serious manifestations, 4 cases of bladder paralysis, 1 of rectal paralysis, 2 of persistent sacral anesthesia, 4 with a severe generalized reaction (pain, vascular hypotension, visceral paralysis, fainting, pallor, sweating and collapse), 2 with generalized convulsions and unconsciousness and 1 with a thrombosed caudal vein. This medium was abandoned after this experience.

The final medium and the one now in use in the Boston City Hospital neurosurgical department is Pantopaque. Four hundred and thirty-four Pantopaque myelograms have been performed on 374 patients with suspected low lumbar and upper sacral root compression. Others in considerable number have also been performed on patients with cord injuries, cord tumors, spinal bony injuries and cervical "disks." Two hundred and thirty-one of the 434 (53 per cent) were verified at operation (Fig. 4). In 29 the operative findings did not agree with the myelographic interpretation. This is an error of 13 per cent. The incidence of unsatisfactory or unreadable films was also 13 per cent (31 out of 231 such myelodence of uninterpreted films (13 compared with 25, 9 and 17 per cent) though significant must be considered correctable. Finally the postmyelographic com-

FIGURE 3. *Skiodan Myelogram — Positive Anteroposterior and Lateral Views (Note Outlining of Individual Roots of Cauda by the Dye).*

plications following the use of Pantopaque in 231 cases was only 15, or 6 per cent. The most serious of these were 1 instance of bladder paralysis, 2 of nausea,

1 of vomiting and 3 of headache. The conclusion that Pantopaque is the safest and nearly the most accurate radiopaque medium that we have used for the myelographic visualization of disk and other lesions causing root or cauda equinal compression in the lower lumbar or upper sacral regions is inescapable.

Diagnosis

It is well known that, in the opinion of many surgeons, it is possible in the group in question to make

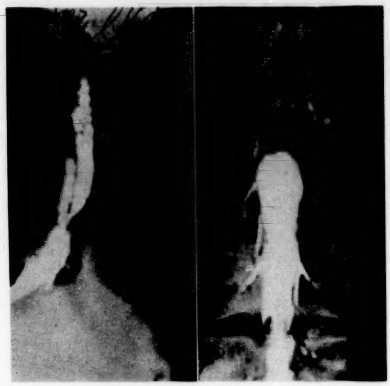

FIGURE 4. *Pantopaque Myelogram — Positive Anteroposterior and Lateral Views.*

an accurate unaided clinical diagnosis of the pathology present and requiring therapy. This is done without such mechanical aids as a myelogram, and such a diagnosis will commonly be described as an extruded or protruded ruptured intervertebral disk. This is not in accord with our experience. Roughly a fifth of our cases without ruptured disks showed the same signs and symptoms that are commonly found in ruptured 4-5 lumbar and lumbosacral disks. The only significant exceptions were patients with pseudarthrosis of the spinous processes and the patient with the thrombosed caudal vein.

This diagnostic unreliability of clinical signs and symptoms has been pointed out in a previous paper.[2] The diagnostic reliability of a myelogram is considered above. It is my belief as the result of this experience that the patient with such suggestive signs and symptoms should be given the benefit of every appropriate diagnostic procedure and in many instances should be offered an exploratory diagnostic operation *after a period of proper conservative therapy,* if he is still disabled by his symptoms and particularly if he has had a previous so-called disk operation. The frequency with which a previous operative scar, a tight dural sheath or root canal or a narrowed spinal canal (all virtually unrecognizable except at operation) have been found to be the sole cause of the original or recurrent symptomatology is too great to be disregarded. As a corollary to this it is essential to determine during the operation, by palpation with an angulated instrument inserted intradurally into the sheath or extradurally into the root canal, whether or not either of these structures is the proximate cause of any compressive radiculitis whether they exist alone or in conjunction with an actual protrusion or extrusion of a nucleus pulposus.

Finally, I would urge that, since we are all victims of our own preoperative diagnostic mental or word pictures of the pathology we believe we are going to correct by our proposed operation, we should make our main primary diagnosis in these patients in terms of root compression as compressive radiculitis or compressive cauda equinitis. These diagnoses should be the justification for our operation. From such a point of view the variable causes of the compression sink, as they should, to a secondary level whether they be a ruptured disk, a tight dural sheath, a previous operation, a tumor or any other cause. Only in this way can we satisfy ourselves that the operation is to be effective and that the *primary* condition has actually been corrected.

This is not a new point of view and has been urged by many other writers. Its value is substantiated by the fact that actual root or cauda equinal compression has been unequivocally demonstrated in 331 of the 375 operations (not compressed — 46, not mentioned — 6) performed on the 545 patients in this series. Further personal evidence in support of this procedure and in denial of the accuracy of unaided symptomatic diagnoses is found in the results of stimulation of lumbar and sacral roots collected during anterior dorsolumbosacral rhizotomies for relief of leg and body spasms in patients with transected spinal cords.[3] Such electric stimulation of individual lumbar and sacral motor roots produces peripheral muscular responses that do not necessarily correspond to the accepted anatomic distribution of the root in question. The only exception is the production of a constant emptying contraction of the bladder, which takes place whenever the second anterior sacral root is stimulated. For example, it is extremely common to elicit a motor response in the muscles of the lower leg and foot in addition to motor responses higher in the leg by stimulation of the third, fourth or fifth anterior lumbar root. This analogue of the long-recognized peripheral overlap in the distribution of the sensory spinal roots is not without its diagnostic importance in the problem at hand.

Conservative Therapy

There can be no doubt that patients complaining of low-back pain, whether classed as industrial or nonindustrial injuries, should be given the benefit of

a long enough period of conservative nonoperative therapy so that the physician in charge can be relatively sure that relief of symptoms and invalidism cannot be cured without operation. Such measures as bed rest, traction, hyperextension of the spine, massage, manipulation, injection of Novocain or its derivatives into spastic muscles, judicious exercise, muscle stretching and muscle building must be given a fair trial. A careful hospital study of other possible causes, such as spondylolisthesis, pseudarthrosis of spinous processes, hernias through the lumbar fascia, tuberculosis, flat feet as well as bad posture, tumors, congenital defects and so forth, must be carried out and the patient's treatment appropriately modified so that these causes can be ruled out. Only then can one properly decide to operate on such a patient for a ruptured disk or a compression of a root or roots. This differential diagnosis necessarily requires the intelligent use of all appropriate nonoperative procedures. Any so-called disk operation that is performed without this preoperative collection of knowledge is, in my opinion, entirely unjustified and the operator can do no more than shoulder the blame for any bad results his patients get if he presumes to operate without this essential preoperative diagnostic study. As a corollary to this it must be recognized that a complete rediagnosis and re-evaluation of the case is obligatory if the patient with low-back symptoms has not been relieved of his invalidism (not his signs or symptoms) at the end of three months of well conceived and executed conservative therapy.

Operation

The first question that the patient wants to have answered once an operation is decided upon is, "Who is to do the operation?" To my mind it makes no difference who is to do the operation *provided* the surgeon can measure up to the requisite minimal standards that will insure an operation that carries a minimal mortality and postoperative morbidity. These standards must include a knowledge of how to get an adequate exposure of and without damage to the compressed root or cauda, with a minimum of local trauma. This, in its turn, requires familiarity with such procedures as opening and closing the dura, the handling of the elements of the cauda equina, all procedures that may be necessary to decompress a root intradurally or extradurally, the control of intradural, extradural and muscular hemorrhage, the recognition and removal of any extradural or intradural neural tumors and experience with working in or near the segmental portion of the central nervous system. With as accurate a preoperative diagnosis as is possible to make with the modern investigative facilities, with a conviction that the operation is incomplete and unjustified if any compressed root or if the cauda is not decompressed and the ability to meet the requirements listed above, any surgically trained nonspecialist or specialist can and should be expected to deal adequately with this segment of the low-back problem.

Operative Technic

There are certain technical aspects of these partial hemilaminectomies that our experience has taught us to regard seriously. The most important is ade-

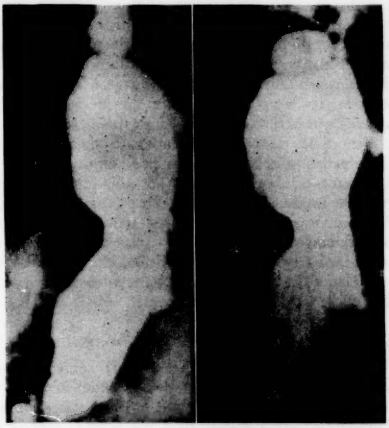

Figure 5. *Pantopaque Myelogram — Deformity Caused by Scar and Verified by Operation — Anteroposterior and Oblique Views.*

quate exposure. This must be governed by the operator's experience and skill. It is axiomatic that too much exposure is harmless and too little exposure immeasurably harmful. The first leaves the patient with an undamaged, decompressed root or cauda, minimal scarring and little if any postoperative symptoms. The second leaves him with a badly contused root, a partially or wholly divided root, an undecompressed root or cauda, extradural and periradicular hemorrhage or scar (Fig. 5) and a wide variety of postoperative symptoms ranging from undiminished pain and invalidism to paraparesis with incontinence of the bladder and bowel, a foot drop and the need for permanent splints.

The Articular Facets

In our experience the crux of the problem of adequate exposure is the operator's willingness to sacrifice, if necessary, the involved articular facets. I do not mean to state or to imply that the facets should be damaged or removed unless adequate exposure and decompression of the root cannot be accomplished otherwise, but I do mean to state that the loss of a pair of intervertebral facets and their intervening

joint space is of infinitely less importance than the continued root compression and inadequate exposure that would result from their retention or undamaged condition. I have reached this conclusion after observing how little if anything the fractured facets have contributed to the loss of stability of seriously fractured vertebras in spine and spinal-cord injuries. Work is now in progress to determine the breaking strength of the articular facets in the lumbar region in order to verify this clinical conclusion. As a corollary to this and other extended similar experience it is my further opinion that the articulating intervertebral facets contribute but little to the lateral stability of the spinal columns in the lumbar region and further that the real stability resides in the multiple strong ligamentous structures that bind the vertebras together at all points and surfaces. If these are not disturbed, no disability per se need be anticipated as the result of damage or loss of the intervertebral articular facets. In the group of patients under study the facets overlying the involved root or root canal were damaged or removed in 130 of 375 operations without discernible weakness or disability of the back or the production of any symptoms other than those that existed prior to their removal.

Operative Hemorrhage

The significance of operative hemorrhage from the point of view of morbidity and the continuation and redevelopment of symptoms and invalidism is equally as important in a different field as adequate exposure is during the operation. The problem seems to be one of hemorrhage after the field has been meticulously left dry and closed. The important and significant clots form deep in the wound and in immediate proximity to the root, the dura and the remains of the ligamentum flavum. If a fusion has been done this acts as an additional nidus. The clot itself does one of three things: it liquefies and forms an uninfected collection of fluid; it liquefies, becomes infected and forms a deep abscess with possible associated osteomyelitis and inevitably an open draining wound, usually in spite of chemotherapy and antibiotics; and, thirdly, as the terminal form of either of the above two, it becomes, with the added complication of an infected foreign-body reaction from any bone graft that has been inserted, an extensive compressive scar with or without bone in it, causing compression of the cauda, one or two adjacent roots, the dura, the arachnoid, the cut bony surfaces of the hemilaminectomy, the muscle, the yellow ligament and often the skin.

We have had much too much of all these complications. We have tried drainage of the wound, instillation of chemotherapeutic agents, parenteral antibiotics, suturing and nonsuturing of the paravertebral muscles, local hot dressings, wide opening of the wound, secondary suture and revision of the wound, immediate postoperative exercise and no exercise in bed, and drainage of the cystic forms by multiple needle punctures and suction. All have helped, and all have failed. When it is all boiled down to fundamentals the first requisite is super-hemostasis, and the second is wide opening of the abscessed or infected wound from wall to wall with, if possible, secondary suture. Indiscriminate use of chemotherapy or antibiotics is useless and indicated only as therapy secondary to the surgical drainage and removal of sequestra and only then if sensitivity tests are appropriate. Indeed, we are convinced that the so-called routine postoperative administration, for example, of penicillin or the instillation or peroral administration of even the most modern chemotherapeutic agents is not only not helpful but definitely harmful in that it distracts the surgeon's attention from the more basic and essential surgical procedures that are still the fundamental requisites for the healing of such an infected wound.

In 375 operations, 6 patients had the ordinary superficial sepsis of the wound without an associated hematoma. This was 1.6 per cent. Twenty-five patients (7 per cent) had hematomas that were recognized and diagnosed. Of these latter 25 hematomas 16 became septic — this was 4 per cent of the total. It is impossible to figure the percentage incidence of postoperative scars. However, 25, or 7 per cent, of the operated patients proved to have scars (Fig. 5) as verified by a second operation. They were shown to have compressed one or more roots or the cauda equina and were all preceded by "disk operations" either at our or other surgeons' hands.

Pathology

The actual pathologic condition that was the cause of the patient's symptoms could be accurately determined only in those cases in which it was actually visualized at operation. Aside from the patients in whom a rupture with protrusion or extrusion of a single fourth-fifth lumbar or of the lumbo-sacral disks were demonstrated, the pathologic cause of the signs and symptoms was as listed below. It should be clearly understood that neither a protrusion nor an extrusion of either of these two disks was considered present or significant unless an accompanying compression of the associated lumbar or sacral root or of the cauda equina could be unequivocally demonstrated.

The pathology found — other than that of protrusion or extrusion of a single fourth-fifth lumbar or lumbosacral disk with its associated root or cauda equina compression — occurred in 166 patients and was as follows: rupture of D12-L1 disk — 1; rupture of L1-2 disk — 1; rupture of L2-3 disk — 2; rupture of L3-4 disk — 7; simultaneous rupture of 2 disks — 5 (L3-4 + lumbosacral — 1, and L4-5 and lumbosacral — 4); no rupture of any disk — 24; compression of root by tight dural sheath — 13; compression of root by tight bony root canal — 16; compression

of cauda equina by narrowed spinal canal — 18; compression of root by scar (of previous operation) — 21; compression of root by scar containing bone (of previous operation with fusion or after bone injury) — 5; compression of cauda equina or root by previous fusion (fusion and scar removed) — 5; other pathology (tuberculosis — 1; adherent cauda equina — 16; lamina on edge with angulation and compression of cauda equina — 1; residual [postoperative] disk material — 4; syphilis — 2; inadequate exposure — root damaged — 3; loose fragment of bone — 1; overlapping spinous processes with pseudarthrosis — 4; thrombosed caudal vein — 1; arachnoidal cyst with compression of cauda — 1; compression of cauda equina by encysted lipiodol — 1; "abnormal disk" — 1; bone wax left from previous operation — 1; spondylolisthesis — 2; rudimentary diastematomyelia — 1; spina bifida — 1; tumor — meningioma — at D8-9 vertebras — 1; inclusion of intradural root filament in dural suture — 1; total — 43).

Attention is particularly drawn to this group of 166 patients whose signs and symptoms justified a preoperative diagnosis of ruptured disk (except for 11 cases) and who were operated upon with that diagnosis but who, upon adequate visualization, proved to have a very different pathologic cause, which could not possibly have been recognized until actually exposed on the operative table.

Operative Complications

Preoperative

There are certain complications that are in existence at the time of the operation, that are sufficiently important and that may not be subject to alteration after the operation, and that warrant attention. Note should be taken of these before the operation as well as of their progress or lack of it following the operation and their presence carefully observed and explained to the patient. In this group these complications occurred as follows: paralysis of both legs —1; paralysis of the bladder—1; and pulmonary tuberculosis—1. The patient with the paralyzed bladder had the same bladder condition afterward that he had previous to the operation. The other 2 recovered.

Postoperative

While the most important postoperative complications in these 375 operations were operative hemorrhage and infection of such hematomas accompanied by sepsis (discussed above) there was another one only a little less important. This was postoperative bladder paralysis. This condition occurred 17 times. It has been impossible to determine in detail what the proximate cause was in all cases, but in many it was unquestionably traceable to compression of the cauda. It had a variable prognosis somewhat dependent on the efficiency of the treatment. We have had our best results with the use of tidal drainage.[4] This is started whenever the patient cannot urinate voluntarily twenty-four hours after the operation. During this first twenty-four hours we are extremely careful to see to it that the bladder is actually emptied of its urine every eight hours. Usually, but not always, following a week or less of tidal drainage, if it is adjusted and checked by repeated cystometrograms, voluntary urination returns. If it does not do so a reestimate of the problem, including a restudy and rediagnosis, is essential and the prognosis must then be made on an individual basis.

There were only 2 cases of thrombophlebitis, 1 of which was complicated by a resultant nonfatal pulmonary embolus. There were 6 cases of increased or new symptomatology developing after the operation and including the patients who either did too much or, what was worse, did too little exercise during their convalescent period. This group does not include the symptoms caused by the compression exerted on roots and cauda by the gradual contraction of a scar. Meningitis (nonfatal) occurred twice — once following wound drainage because of excessive operative bleeding and the other time as one of the manifestations of a generalized septicemia in a streptococcus carrier.

Three roots were divided by the operator, one in each of 3 operations. In every instance, the basic reason was inadequate exposure.

Three patients exhibited temporary paresis of one leg, and 1 other developed a permanent atrophy of one lower leg that required the use of a foot-drop brace.

Fusion

I feel strongly that a fusion of the spine in the compressed root area has no therapeutic relation to the causative ruptured intervertebral disk, tight root sleeve and so forth. Nor does the theory that the vertebras are looser in relation to each other in this area stand up under critical examination. Such predicated looseness must, of necessity, involve a varying degree of destruction or stretching of such ligamentous structures as the anterior and posterior vertebral body ligaments, the interspinous, interlaminal and interpeduncular ligaments and the yellow ligament. Partial destruction of any or all of these ligaments puts the patient into the category of severe vertebral and cord or cauda injury, which is entirely different from the problem at hand. Other stretching of these ligamentous structures implies a prolonged gradual process such as the change in vertebral relation seen in spondylolisthesis. The presence of such a condition as a protruded or extruded disk can bear no therapeutic relation to the need or lack of need for fusion in patients with spondylolisthesis or other slowly progressive alterations of the adjoining vertebral relations.

The function of the intervertebral articular facets may be completely disregarded in so far as the maintenance of the stability of the spine is concerned as discussed above. The theory that motion in the joint existing between any two adjacent facets is the cause of pain lacks adequate evidential support, but, even if it were so, a better method of treatment would be to excise both facets rather than to attempt immobilization by destruction of the joint surface or the insertion of a foreign body such as a metal screw or bolt.

We have recommended that only 3 of our 545 patients have fusions performed on them. Two of these 3 had a spondylolisthesis and were relieved by the fusion. The other was an early and erroneous recommendation and as far as we know did no good. Fusion was advised by an orthopedic consultant in 1 other case — I do not know whether it was ever performed. Only 2 (other) of our patients were fused as part of and after the neurosurgical operation. One of these left the hospital without symptoms seventeen years ago and has not been heard of since. The other was referred for fusion eight years after the original hemilaminectomy because his symptoms still persisted. In comparison with this experience we have removed for adequate cause fusions or bone grafts put in elsewhere in 12 patients. The results have been very disappointing in terms of relief of persistent invalidism, ability to work and neurosis. This is understandable once the amount of scar, overgrowth of bone, intradural adhesions, compression of roots and cauda and extradural, muscular and even cutaneous adhesions have been seen at operation and an attempt made to correct such conditions. I am convinced that it is much better to reserve fusions, bone grafts, the use of metal screws, bolts and wires for those cases in which the indications for such procedures exist alone. Certainly, no fusion or graft operation should be done for the purpose of removing a protruded or extruded nucleus pulposus or of decompressing a spinal root or the cauda equina as a part of or at the same time as a hemilaminectomy. It is quite time enough to carry out such an elective procedure three to six months after the hemilaminectomy and because of the indications inherent in nothing but the demonstrated need for a fusion.

Convalescent Care

In my experience the convalescent care of patients that have been adequately operated upon for compressive radiculitis is as important as the operation in so far as remission of invalidism and return to work goes. There can be little dispute with the point of view that in such patients the paraspinal muscles before operation are in spasm and anatomically shortened. They have a varying degree of atrophy of disuse and are therefore weak. The supporting vertebral ligaments are required to do more than they were constructed to do, and back motion is splinted and painful. There is almost always present the continuous nagging pain of an irritated compressed spinal root with resultant concentration of the patient's attention on this rather than his work. Finally, virtually complete invalidism and lack of muscular effort with a high degree of psychoneurosis develops. This is heightened further by the fact that almost always he has had attacks similar to the one that led to the operation but has previously recovered from them even though the doctors offered no effective therapy and indeed often insisted that he waste time, effort and money in treatment that he himself was convinced was useless, an opinion that had been borne out by his experience through the years. In short these conditions require postoperative convalescent therapy, which must first stretch and strengthen the shortened weak muscles locally, must simultaneously provide a method of rebuilding the body and its more active functions generally and finally must do so by the patient's own efforts. Only in this way will the patient be persuaded to be co-operative and intelligent about his problem and at the same time have no one to blame or to provide an alibi for him in case of failure, except himself. Only thus can permanent invalidism, neurosis and a whole train of similar disabilities be done away with.

Along with this positive point of view there is an equally important negative attitude. Certain procedures must *not* be carried out on these patients. The more important follow; no formal exercise while the patient is bed ridden after operation. There is too much danger of unrecognizable deep hemorrhage with a resultant scar. Patients must not get out of bed later than eight or nine days but then must start active ambulation; they must not be discharged from the hospital until they can walk up and down two flights of stairs in succession. Their formal convalescent regimen must not be started until after they have been home for two weeks. Light therapy, diathermy, massage, passive and assisted active motion, whirlpool or other baths and synthetic exercise in any form are not only contraindicated but in my experience have been definitely harmful. If any local muscle-building exercises are needed they must be done by the patient himself in such a way as to mimic normal functional use and activity.

After his two weeks at home the patient should report back to his surgeon. The latter can then outline a convalescent regimen that will meet the fundamental requirements as stated above. I find that I can accomplish all that is necessary along these lines by explaining to the patient that, to stretch his shortened, still spastic muscles he must bend at his waist forward, backward and to either side ten times every morning right after he gets out of bed. More bending than this is harmful and less is ineffectual in any twenty-four-hour period, provided that at each bend the patient goes far enough to feel his back and thigh

muscles stretch, that he keep his knees straight and that he have his hands on his hips. He is also told to take walks, which must be gradually increased in length until he is walking 5 miles twice every day. These walks must each be of such length that the patient is not exhausted but does feel that he has had definite progressively greater and greater exercise.

He should report to his surgeon not oftener than once in every two or three weeks and should be physically in condition to return to work in eight to ten weeks after leaving the hospital. He should develop no neurotic tendencies and should be willing and will be physically able to do any kind of job that does *not require* lifting, jumping, pulling or pushing or working with his back in a strained unnatural position for even relatively short periods. These limitations will apply for the rest of his life, at work and at home. They are designed to prevent the recurrence of any condition that can produce a compressive radiculitis, to prevent the redevelopment of spasm in any of the bodily musculature and to make the patient personally responsible for his own recovery and welfare and thus deprive him of the opportunity of using alibis provided by others, and yet prevent him from being put or from putting himself into such positions as have already been demonstrated to be unfavorable to his physical welfare. It should be repeated that this convalescent treatment is predicated on the assumption that the previously compressed root or roots have been decompressed. If they had not been, no variety or amount of convalescent therapy will relieve the patient of his symptoms, stop his invalidism or return him to gainful labor.

Deaths

Four patients died. All had been operated upon. This was an operative mortality of 1 per cent (4 out of 375) and a case mortality of seven tenths of 1 per cent (4 out of 545). Two were autopsied, and the other 2 not. Of the 2 autopsied patients 1 died of a transfusion kidney caused by the use of improperly matched blood given as a postoperative prophylactic transfusion, and the other of miliary tuberculosis, which developed after what had been believed to have been an ordinary jujitsu disk was removed, but which, when removed, turned out to be intervertebral tuberculosis. The other deaths, while not verified by autopsy, presented abundant clinical evidence to support the diagnoses that were reached. One patient was determined by culture to be the carrier of a very virulent streptococcus, which remained under control until the patient was subjected to the trauma of the operation. The combination was too much for him. Before his death, which occurred three days after operation, blood-stream, wound and nose and throat cultures all grew out an identical bacterium. The other patient died without ever leaving the hospital, of arteriosclerosis, vascular hypertension and cardiorenal disease, severe gastrointestinal hemorrhages being the immediate cause of death three years after operation at the age of seventy-three.

Summary and Conclusions

This is a report of a clinical investigation carried out over seventeen years on 545 patients who either had or were believed to have had a low lumbar and upper sacral compressive radiculitis. This was most frequently caused by a ruptured intervertebral disk with protrusion or extrusion of a nucleus pulposus, but other changes causing the radiculitis were found to be almost as important. Various aspects of the diagnosis, the operative technic, the intervertebral facets, postoperative complications, convalescent care, fusion and hospital end results are considered.

The commonest fundamental cause of injuries leading to a lumbar or upper sacral compressive radiculitis or cauda equinitis was *"lifting,"* the next commonest *"a fall"* and the third commonest was undetermined and was listed as *"no cause."*

The overwhelmingly usual history of patients such as these, in regard to their low-back signs and symptoms, is that of an initial back injury with recovery after conservative therapy and followed months or years later by a succession of similar back injuries, each of which has more and more signs and symptoms and each of which is followed by greater and greater invalidism and less and less relief from conservative therapy. The majority of these patients come to "advised" or "actual" operative therapy in the two years after their initial injury. The industrial factor that may be present in the original injury plays no part in the above data.

The best medium to use in doing myelograms is Pantopaque. Four hundred and thirty-four such myelograms were performed. In 53 per cent the operative findings agreed with the preoperative myelographic diagnosis; in 13 per cent the findings disagreed, and in 13 per cent the films were technically unreadable. The incidence of postmyelographic complications was 6 per cent.

Lipiodol, air and the water-soluble substance Skiodan were all tried but discarded for the following reasons: lipiodol — too high a percentage of error and unreadable films; air — the same as lipiodol; Skiodan—too high a percentage of serious postmyelographic complications.

It is my strong conviction that the primary diagnosis or the diagnosis that justifies operation in this group of patients should be compressive radiculitis of (naming root involved) or compressive cauda equinitis. The estimated cause of the compression should be relegated to an inferior diagnostic position.

The two most important technical considerations in regard to operations done on these patients are: first, adequate exposure involving, if necessary, the damage

or removal of the intervertebral facets and, second, "super-hemostasis." The second is primarily dependent on the first.

Our evidence strongly suggests that the stability of the lumbar spine resides only in the ligamentous structures binding the vertebral bodies, pedicles, laminas and spinous processes together.

An overlooked but extremely important pathologic finding in this series and hence in other similar series is the number of cases in which a root compression is found but not corrected either alone or in conjunction with a protruded or extruded nucleus. It has been our custom for some years to open the dural root sheath, ascertain its capacity in relation to the size of the included root by instrumental palpation and then do the same thing to the intervertebral foramen. Compressed roots are decompressed by splitting the dural sheath lengthwise or by a foraminotomy or both.

Our greatest postoperative complication and the most difficult one to control has been the development of hematomas deep in the wound with their consequent and resultant scars, compressions, adhesions, sepsis and so forth.

I consider fusion absolutely contraindicated as a part of the hemilaminectomy done to relieve the compression of the root or cauda. If it is indicated three to six months later on adequate evidence, it will be quite time enough to perform it then. We have felt justified in recommending fusion as part of the necessary therapy in only 3 out of 545 patients, and do not believe it is ever justified except for specific detailed indications that have only to do with fusion.

A description of a satisfactory regimen of postoperative convalescent care is given.

The operative mortality in 375 operated patients was 1 per cent. The case mortality of the entire series was seven tenths of 1 per cent.

References

1. Munro, D., and Elkins, C. W. Two-needle spinal myelography: new technique for visualization of spinal subarachnoid space. *Surg., Gynec. & Obst.* **75**:729-736, 1942.
2. Munro, D. Diagnosis of posterior herniation of lumbar intervertebral disks. *New Eng. J. Med.* **232**:149-160, 1945.
3. *Idem.* Rehabilitation of patients totally paralyzed below waist: with special reference to making them ambulatory and capable of earning their living. I. Anterior rhizotomy for spastic paraplegia. *New Eng. J. Med.* **233**:453-467 and 731, 1945.
4. *Idem. The Treatment of Injuries to the Nervous System.* 284 pp. Philadelphia: Saunders, 1952. Pp. 82-118.

HORMONAL INFLUENCES ON THE GROWTH AND PROGRESSION OF CANCER*

Tests for Hormone Dependency in Mammary and Prostatic Cancer

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THE inter-relation between the sex hormones and certain forms of cancer was first appreciated by Schinzinger[1] in 1889, and demonstrated in man by Sir George Beatson,[2] who carried out ovariectomy for carcinoma of the breast and obtained a remission of the disease. This work was soon confirmed by others,[3] and by 1905, Lett[4] was able to report a series of 99 cases of inoperable carcinoma of the breast treated by oöphorectomy. In this series he observed that a good clinical response occurred in 41 per cent of the patients younger than fifty years of age but in only 23 per cent of those over fifty. It is of interest that these figures, which reflect the number of tumors that will respond favorably to gonadectomy and, therefore, are assumed to be hormone dependent, have been confirmed subsequently by many workers in the field.[5-7]

The advent and ready accessibility of the synthetic sex hormones in the past sixteen years has led to their use in the attempt to control the progress of neoplastic disease.[8-10] The rationale of the modern palliative treatment of advanced carcinoma of the mammary and prostate glands by endocrine therapy is based on the alteration of the hormonal environment of the cancer cell. It can be postulated that by administration of the appropriate hormone—whether it is estrogen, androgen or cortisone—or by its removal by castration, adrenalectomy or hypophysectomy, the tumor-host relation is altered in favor of the host, and an increase in resistance to the growth of the tumor cells results. In the present state of knowledge the results of hormone therapy are unpredictable[11]; for example, in the treatment of carcinoma of the breast in premenopausal women, testosterone propionate generally produces both better subjective and objective remissions than stilbestrol, whereas in postmenopausal women, estrogens are more frequently effective. On the other hand, in a certain proportion of patients in both age groups estrogenic substances may increase the rate of tumor growth.[12] It appears that in such cases the tumor cells are dependent upon and being stimulated by the administered estrogens.

Pincus and Graubard,[13] in 1941, demonstrated that postmenopausal women with carcinoma of the breast excreted more estrogens in their urine than normal postmenopausal women. This finding has recently been confirmed by Dao[14] and by Smith and Emer-

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son.[15] Appreciating the significance of animal experiments in which castration of guinea pigs and mice at birth[16,17] led to adrenal hypertrophy and adrenocortical tumors, Huggins and Scott[18] postulated that patients with cancer, particularly those who were postmenopausal or had been castrated, might have the growth of the tumor stimulated by the excessive production of adrenal sex hormones. In 1943 they first attempted bilateral adrenalectomy for cancer of the prostate. When cortisone became available, adequate supportive therapy made this procedure feasible. Since then several series of cases have been reported in which carcinomas of the breast and prostate were treated with bilateral adrenalectomy, remarkably similar results being obtained by different investigators.[19-23] It seemed that between 30 and 40 per cent of patients gave a good objective response and that the remainder were unaffected or made worse by the operation. Patients who responded presumably had hormone-dependent tumors and had usually derived benefit from preceding gonadectomy. These results reinforced the views expressed by earlier workers that a similar proportion were dependent on the stimulating effect of circulating sex steroids and that the remaining cases pursued either an autonomous course or else were under the control of some other hormone, perhaps produced by the pituitary gland, such as growth hormone.

The selection of tumors that will respond to gonadectomy or bilateral adrenalectomy has become of critical importance because it is on such patients that operation must be advised; the remainder should be spared the operative mortality and the associated considerable morbidity. Attempts at selection hitherto have been made as follows:

Study of the results achieved by previous hormonal alteration — for example, patients who obtained a good clinical remission with gonadectomy will probably benefit from adrenalectomy.

Study of the histologic type of the primary tumor. Huggins and Scott[18] believe that in carcinoma of the breast, the adenocarcinomas will respond to adrenalectomy because these cells are more highly differentiated and, therefore, more readily controlled by circulating estrogens. Other workers[15,17] do not agree and regard the histologic type of the primary tumor as bearing no relation to the result achieved.

It is obviously desirable to find more practical and reliable methods of selection. In patients with osseous metastases the study of the calcium excretion in the urine could be used in such a way. The observation that hypercalcemia and hypercalcinuria occur spontaneously in 10 per cent of patients with osseous metastases was made by Griboff et al.[24] and Herrmann and his associates.[25] Pearson and his co-workers[26-28] were the first to show a fall in urinary calcium levels after ovariectomy. We have confirmed this finding on numerous occasions; a typical example is shown in Figure 1. The initial hypercalcinuria and the prompt fall that followed ovariectomy, together with the relief of bone pain experienced in the postoperative period in this case, is a good indication that the tumor is hormone dependent and that further attempts at

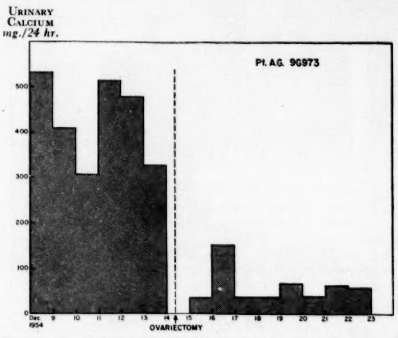

FIGURE 1. *Effect of Ovariectomy on Urinary Calcium Excretion in A.G., a Fifty-three-Year-Old Woman.*

Radical mastectomy was performed for carcinoma of the left breast in November, 1951; x-ray castration was carried out in July, 1953, when osseous metastases were demonstrated. Testosterone produced temporary improvement but by December, 1954, the symptoms were worse, and ovariectomy was performed. Calcium excretion was markedly reduced by ovariectomy in this case, suggesting decreased rate of tumor growth as a result of withdrawal of ovarian estrogens.

hormonal suppression are likely to be successful. Direct evidence for the relation of ovarian activity to tumor growth is shown by the measurement of urinary estrogen excretion. This was determined by the bioassay method of Smith and Smith, employing both hydrolysis with acid alone (To) and acid with zinc (Tzn).[29] Preoperative levels were 217 International Units for the former and 224 International Units for the latter. Postoperatively, these values fell to less than 50 and to 117 International Units respectively. It is noteworthy that x-ray castration had not completely suppressed ovarian hormone production.

Extending these observations further, Pearson et al. pointed out that the converse was true — namely, that in some patients by stimulation of the tumor with a variety of hormones, high levels of urinary and serum calcium could be produced and used as an index of the hormone dependency of the tumor. Thus, by study of the changes in the urinary calcium excretion an accurate prediction of the likely efficacy of any proposed alteration of hormonal balance can be made.

Sex-Hormone-Stimulation Test

The following test has been devised to accomplish this purpose: the patient is placed on a maximal in-

take of 200 mg. of calcium, and the daily twenty-four-hour urinary calcium excretion is determined. We have employed the method of Clark and Collip[30] for calcium analysis. A normal subject on this intake will excrete about 50 to 100 mg. of calcium a day in the urine. This will rise if osteolysis is occurring. It can be calculated that when 1 gm. of bone is destroyed by neoplastic tissue about 100 mg. of calcium is liberated and excreted in the urine.

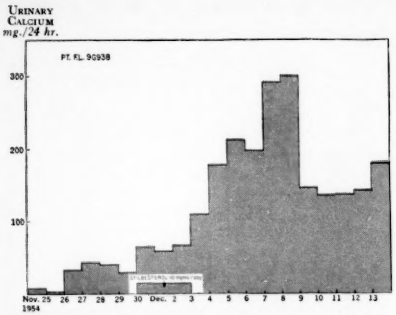

FIGURE 2. *Effect of Administration of Stilbestrol in F.L., a Fifty-five-Year-Old Woman.*

Radical mastectomy for carcinoma of the left breast was performed in 1951. She remained well until January, 1954, when osseous metastases were demonstrated. She responded to testosterone therapy, but by December, 1954, her condition had deteriorated and she was admitted to the hospital for evaluation of hormone dependency of the tumor. The administration of stilbestrol, 10 mg. a day, over a three-day period, resulted in a marked exacerbation of clinical symptoms and an increase in the urinary calcium excretion, from approximately 50 mg. a day to levels between 200 and 300 mg. a day. The combination of calcium changes and symptomatic reaction constitutes strong evidence that the tumor was estrogen dependent.

After a control period of five to seven days a provocative dose of hormone is administered. In prostatic cancer a dose of 100 mg. of testosterone propionate intramuscularly is given daily for three consecutive days, and in carcinoma of the breast the equivalent of 5 to 10 mg. of stilbestrol is administered over a similar period. A positive response indicating hormone dependency of the tumor is judged in two ways: a mobilization of calcium from the skeleton causing hypercalcinuria and sometimes hypercalcemia; and a systemic reaction characterized by malaise, increase in bone pain, pyrexia and lethargy.

The rapidity of onset, extent and duration of the hypercalcinuria appears to depend both on the degree of hormone dependency of the tumor, for all tumors may not be equally dependent, and the extent and size of the osseous metastases. When there are very few bony metastases it is obvious that even if they all become active and grow under hormonal stimulation the resultant bone destruction and increased urinary calcium excretion will be relatively small. On the other hand, if soft-tissue metastases predominate over osseous, the systemic reaction will be more prominent than the calcium mobilization. In the usual positive response to this test the rise in urinary calcium will occur within two or three days of the "stimulation" and may persist for several weeks. A typical response is presented in Figure 2. This patient with extensive osseous metastases from carcinoma of the breast showed both the systemic reaction and hypercalcinuria.

The systemic reaction may be very severe and may call for an emergency ovariectomy or adrenalectomy. Once this operative intervention has occurred the endogenous source of stimulating hormone is removed, and the patient may never show the expected hypercalcinuria. An example of this occurrence is shown in Figure 3. The severe systemic reaction coupled with the postoperative precipitous fall in urinary calcium excretion denotes hormone dependency even though no hypercalcinuria was observed in the short interval between stimulation and ovariectomy.

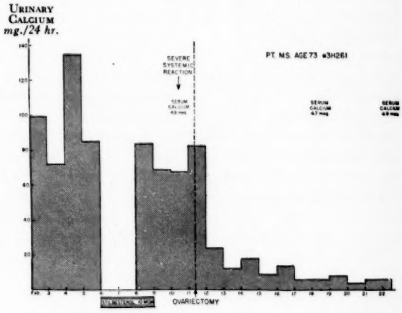

FIGURE 3. *Effect of Estrogen Activity on Urinary Calcium Excretion in M.S., a Seventy-three-Year-Old Woman.*

In November, 1954, a carcinoma of the left breast, with multiple skeletal metastases, was found. She was admitted to the hospital for evaluation of the hormone dependency of the tumor, and a stimulation test was carried out. In this case stilbestrol administration did not increase urinary calcium excretion or serum calcium concentration. A severe systemic reaction did occur, however, requiring ovariectomy for control. After the operation the calcium excretion decreased considerably, and this was associated with clear-cut clinical improvement. It should be emphasized that under most other circumstances (not involving tumor growth) the withdrawal of estrogen in older women results in an increased rather than a decreased rate of urinary calcium excretion.

CORTISONE-INHIBITION TEST

A decision has to be made whether or not adrenalectomy should be carried out on patients who have already undergone gonadectomy and have subsequently shown an exacerbation of their disease. One

can obtain considerable help in these cases by observing the rate of urinary calcium excretion when adrenocortical activity is suppressed with cortisone. An example of successful cortisone suppression is indicated in Figure 4 by the fall in urinary calcium level. The significance of this observation is established by the fact that the calcium excretion remained low in the postadrenalectomy period.

An unsatisfactory response to adrenocortical suppression is shown in Figure 5. Owing to the failure of fluorohydrocortisone to induce a fall in urinary calcium or symptomatic improvement in this case it was

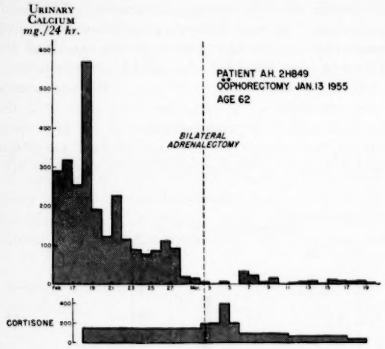

FIGURE 4. *Effect of Cortisone Inhibition of Adrenocortical Activity on Urinary Calcium Excretion in A.H., a Sixty-two-Year-Old Woman.*

Radical mastectomy for carcinoma of the right breast was performed in June, 1953. In September, 1953, she was shown to have osseous metastases in the lumbar spine, for which she received x-ray therapy. She remained well until three months before admission, when her symptoms of bone pain increased, and on admission widespread osseous metastases were found. An estrogen-stimulation test produced a severe systemic reaction and a rise in excretion of urinary calcium. An ovariectomy was carried out, with marked symptomatic improvement. The urinary calcium, however, did not fall to normal levels, and this was regarded as evidence of continuing activity of the disease. Bilateral adrenalectomy was considered advisable, and to assess the efficacy of this treatment a cortisone-inhibition test was carried out. Under the influence of cortisone the urinary calcium excretion decreased to some extent and the patient felt better. After adrenalectomy had been performed, the satisfactory reduction in urinary calcium excretion and symptomatic remission were maintained.

predicted that bilateral adrenalectomy would not produce a remission of the disease. This proved to be the case, and although a transient fall in urinary calcium did follow adrenalectomy the patient's symptomatic improvement was slight and it was the impression that the progress of the disease had been halted little if at all.

In patients who are exhibiting severe symptoms of their disease the use of the cortisone-suppression test is preferable to a hormone-stimulation test to avoid the possibility of dangerous aggravation of the existing symptoms.

SUMMARY OF RESULTS

The results of 7 estrogen-stimulation tests are pre-

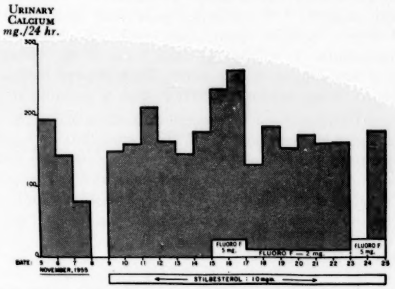

FIGURE 5. *Unsatisfactory Response to Adrenocortical Suppression in E.B., a Fifty-four-Year-Old Man.*

Pain developed in the left hip in March, 1952, and the patient was found to be suffering from carcinoma of the prostate, with multiple skeletal metastases. He was placed on stilbestrol therapy but derived little benefit from this and from orchiectomy, which was carried out in March, 1953. The disease progressed symptomatically and objectively, and in November, 1954, he was admitted to the hospital for evaluation. The studies showed that on stilbestrol, both with and without the addition of fluorohydrocortisone, urinary calcium excretion was unchanged.

sented in Figure 6. Each column in this and the following figures represents the average daily urinary calcium excretion measured over a period of three or more days, starting at least three days after the begin-

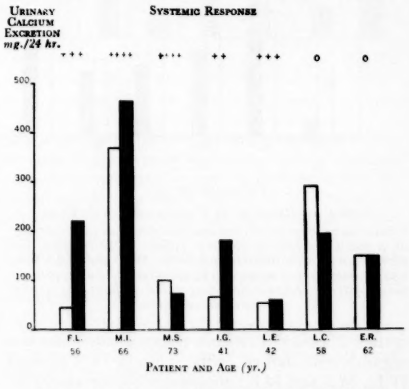

FIGURE 6. *Estrogen-Stimulation Tests in 7 Cases.*

Each column represents the average daily urinary excretion on a calcium intake of 200 mg.; (white column before, and dark column during and after the administration of 5-10 mg. of stilbestrol daily for three days). It will be noted that in 3 cases there was a clear-cut increase in urinary calcium excretion on stilbestrol. In all these, systemic reaction was marked. In addition, 2 patients (M.S. and L.E.) showed little significant change in calcium excretion but did have a considerable systemic response. In L.C. there was suggestive evidence that the administration of estrogen reduced the growth rate of the tumor.

ning of a diet containing not more than 200 mg. of calcium. In judging the systemic reaction the following criteria have been used: +, malaise; ++, malaise and pain; +++, malaise, pain and fever; and ++++, malaise, pain, fever, lethargy, coma or convulsions. It will be seen that 5 out of the 7 tests have been judged to be positive. Three showed both a rise in urine calcium excretion and a systemic response; 2 showed a systemic response only. The two negative tests showed neither change. In 3 patients (F.L., M.I. and M.S.) subsequent oöphorectomy resulted in definite clinical improvement, as would be predicted from the estrogen-stimulation test. Patients I.G. and L.E. had already undergone ovariectomy, and it was not carried out in patients L.C. and E.R. because of their negative stimulation test. This small series does not reflect, of course, the true numerical relation of hormone-dependent to nondependent tumors.

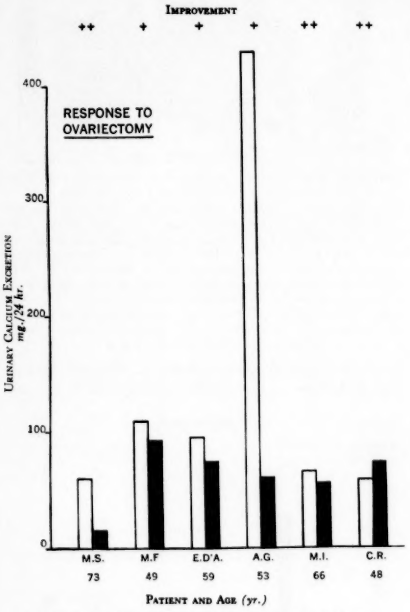

FIGURE 7. *Response to Ovariectomy in 6 Cases.*

Each column represents the average daily urinary excretion on a calcium intake of 200 mg. (white column before, and dark column after ovariectomy). In M.S. and A.G. there was a great reduction in calcium excretion. In several patients systemic improvement was noted without any change in calcium excretion.

The changes in calcium excretion after ovariectomy in 6 patients are shown in Figure 7, together with the degree of subjective and objective improvement. In 2 of these (M.S. and M.I.) estrogen-stimulation tests had been done and were found to be positive (Figure 6).

Of these 6 patients 2 exhibited highly significant and 2 others equivocal diminution in urinary calcium excretion; all showed subjective improvement. It is particularly noteworthy that ovariectomy may bring about improvement long after the menopause. Patient M.S. is of special interest in this regard since at the age of seventy-three, she is in the age group that Nathanson[9] believed may be benefited by estrogen therapy. As shown previously in Figure 6, however, her tumor was still estrogen dependent. Moreover, measurement of her urinary estrogen excretion preoperatively revealed the remarkably high levels of To, 1330, and Tzn, 2800 International Units. Postoperatively, these values fell to 50 and 125 International Units respectively. It must be recognized that the degree of clinical improvement may be out of proportion to the change in urinary calcium excretion. Further studies are being done to determine the correlation of improvement with urinary estrogen excretion.

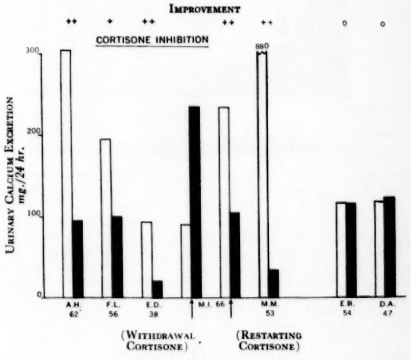

FIGURE 8. *Effect of Cortisone Inhibition on Urinary Calcium Excretion in 8 Cases.*

Each column represents the average daily excretion on a calcium intake of 200 mg. (white column before, and dark column after administration of cortisone, 50-100 mg. daily except in M.I., as indicated). It will be noted that in 5 of the 8 cases there was a marked reduction in urinary calcium excretion on the administration of cortisone. In M.I. the sensitivity to cortisone was exhibited both by its withdrawal and by its readministration.

The effect of adrenal suppression with cortisone upon urinary calcium excretion in patients previously castrated and under investigation to determine the advisability of adrenalectomy is shown in Figure 8. The criteria used in judging improvement, as shown in this figure, are as follows: +, decrease in bone pain; and ++, decrease in bone pain and healing of

metastases as shown by x-ray and physical examination. Five out of 7 had a positive response to cortisone inhibition. In M.I., who had been on cortisone suppression, urinary calcium excretion rose when the cortisone was withdrawn and returned to the previous level when its administration was resumed. Two negative tests were seen, no change occurring in urinary calcium excretion and no improvement in symptoms. Figures 9 and 10 present the combined data on 5 patients studied before and after each sequential step in therapy.

It may be seen that the rate of calcium excretion in the urine may increase both after estrogen administration and also with the passage of time. This relatively simple measurement thus becomes useful not only in evaluating the degree of hormone dependency of any given tumor but also in assessing its rate of inherent growth.

Discussion

There has hitherto been no satisfactory method for the selection of cases of mammary and prostatic cancer that will respond favorably to gonadectomy or adrenalectomy. The present study suggests that in patients with osseous metastases, by observing the urinary calcium levels before and after a hormone-stimulation or adrenocortical-suppression test, one can obtain definite assistance in assessing the hormone dependency of the tumor. In this way cases suitable for operation can be selected, and the remaining patients with autonomous tumors will be spared the mortality and morbidity that are coupled with ovariectomy and adrenalectomy.

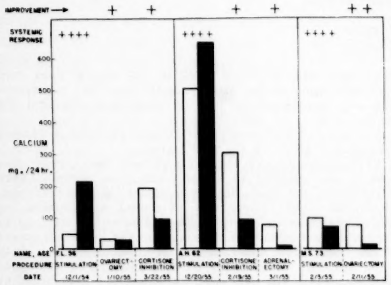

FIGURE 9. *Effect of Various Procedures on Urinary Calcium Excretion.*

Each column represents the average daily excretion on a calcium intake of 200 mg. (white column before and dark column after the procedure indicated). Study of these cases indicates the varying response to estrogen stimulation, ovariectomy, cortisone inhibition and adrenalectomy. In each case depicted, a positive estrogen-stimulation test or cortisone-inhibition test is associated with improvement in symptoms or diminution in calcium excretion or both after ovariectomy or adrenalectomy.

It is imperative that the surgeon maintain constant strict supervision of these tests and that if untoward symptoms occur, particularly after the stimulation test, it be terminated and the surgeon be prepared to carry out an "emergency" gonadectomy or bilateral adrenalectomy.

Summary

A review of the development of the hormone treatment of carcinoma of the breast and prostate is made, and the need for selection of cases that are hormone dependent is emphasized.

Two methods are described by which such hormone dependency may be evaluated: the sex-hormone-stimulation test, in which results are assessed by observation of the increase in urinary calcium excretion and subjective symptoms; and the cortisone-inhibition test, in which the result is judged by the decrease in urinary calcium excretion and improvement in subjective symptoms.

Examples of these tests are shown, and the results correlated with the clinical response to ovariectomy and adrenalectomy.

We are indebted to Dr. J. Hartwell Harrison, who performed the adrenalectomy, and to Drs. J. E. Dunphy, Somers H. Sturgis and Carl W. Walter, who performed the ovariectomies in the cases reported.

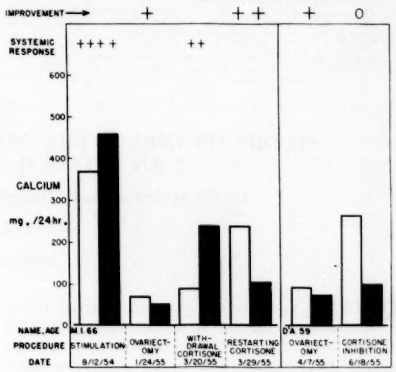

FIGURE 10. *Same Data As in Figure 9.*

References

1. Schinzinger, Das Karzinom der Mamma. *München. med. Wchnschr.* **52**:1724, 1905.
2. Beatson, G. T. On treatment of inoperable cancer of mamma: suggestions for new method of treatment with illustrative cases. *Lancet* **2**:104-107 and 162-165, 1896.
3. Boyd, S. On oöphorectomy in cancer of breast. *Brit. M. J.* **2**: 1161-1166, 1900.
4. Lett, H. Analysis of 99 cases of inoperable carcinoma of breast treated by oöphorectomy. *Lancet* **1**:227, 1905.
5. Adair, F. E., et al. Use of estrogens and androgens in advanced mammary cancer: clinical and laboratory study of 105 female patients. *J.A.M.A.* **140**:1193-1200, 1949.
6. Douglas, M. Treatment of advanced breast cancer by hormone therapy. *Brit. J. Cancer* **6**:32-45, 1952.

7. Dresser, R. Effect of ovarian irradiation on bone metastases of cancer of breast. *Am. J. Roentgenol.* **35**:384-388, 1936.
8. Nathanson, I. T. Effect of stilbesterol on advanced cancer of breast. *Cancer Research* **6**:494, 1946.
9. *Idem.* Influence of stilbesterol on advanced cancer of breast. *J. Clin. Investigation* **25**:930, 1946.
10. Haddow, A., Watkinson, J. M., Paterson, E., and Koller, P. C. Influence of synthetic oestrogens upon advanced malignant disease. *Brit. M. J.* **2**:393-398, 1944.
11. Nathanson, I. T. Clinical investigative experience with steroid hormones in breast cancer. *Cancer* **5**:754-762, 1952.
12. Committee on Research, Council on Pharmacy and Chemistry, American Medical Association. Personal communication.
13. Pineus, G., and Graubard, M. Estrogen metabolism in cancerous and noncancerous women. *Endocrinology* **26**:427-432, 1940.
14. Dao, T., L-Y. Estrogen excretion in women with mammary cancer before and after adrenalectomy. *Science* **118**:21, 1953.
15. Smith, O. W., and Emerson, K., Jr. Urinary estrogens and related compounds in postmenopausal women with mammary cancer: effect of cortisone treatment. *Proc. Soc. Exper. Biol. & Med.* **85**: 264, 1954.
16. Spiegel, A. Über das Auftreten von Geschwülsten der Nebennierenrinde mit vermännlichender Wirkung bei frühkastrierten Meerschweinchenmännchen. *Virchows Arch. f. path. Anat.* **305**:367-393, 1939.
17. Wooley, G. W., and Little, C. C. Incidence of adrenal cortical carcinoma in gonadectomized male mice of extreme dilution strain. *Cancer Research* **5**:211-219, 1945.
18. Huggins, C., and Scott, W. W. Bilateral adrenalectomy in prostatic cancer: clinical features and urinary excretion of 17-ketosteroids and estrogen. *Ann. Surg.* **122**:1031-1041, 1945.
19. Taylor, S. G., Li, M. C., Eckles, N., Slaughter, D. P., and McDonald, J. H. Effect of surgical Addison's disease on advanced carcinoma of breast and prostate. *Cancer* **6**:997-1009, 1953.
20. Pearson, O. H., Whitemore, W. F., Jr., West, C. D., Farrow, J. H., and Randall, H. Clinical and metabolic studies of bilateral adrenalectomy for advanced cancer in man. *Surgery* **34**:543-546, 1953.
21. Cade, S. Adrenalectomy for breast cancer. *Brit. M. J.* **1**:1-4, 1955.
22. Harrison, J. H., Thorn, G. W., and Jenkins, D. Total adrenalectomy for reactivated carcinoma of prostate. *New Eng. J. Med.* **248**:86-92, 1953.
23. Pyrah, L. N., and Smiddy, F. G. Mammary cancer treated by bilateral adrenalectomy. *Lancet* **1**:1041-1047, 1954.
24. Griboff, S. I., Herrmann, J. B., Smelin, A., and Moss, J. Hypercalcemia secondary to bone metastases from carcinoma of breast: relationship between serum calcium and alkaline phosphatase values. *J. Clin. Endocrinol.* **14**:378-388, 1954.
25. Herrmann, J. B., Kirsten, E., and Krakauer, J. S. Hypercalcemic syndrome associated with androgenic and estrogenic therapy. *J. Clin. Endocrinol.* **9**:1-12, 1949.
26. Pearson, O. H., West, C. D., and Treves, N. Role of ovarian function in growth of mammary carcinoma in man. *J. Clin. Investigation* **32**:594, 1953.
27. Pearson, O. H., and West, C. D. Objective methods of management of tumor growth in man. *Proc. Am. A. Cancer Research* **1**:42, 1953.
28. Pearson, O. H., West, C. D., Hollander, V. P., and Escher, G. C. Alterations in calcium metabolism in patients with osteolytic tumors. *J. Clin. Endocrinol.* **12**:926, 1952.
29. Smith, O. W., and Smith, G. V. Increased estrogenic potency of human urine after zinc-hydrochloric acid hydrolysis. *Endocrinology* **28**:740-746, 1941.
30. Clark, E. P., and Collip, J. B. Study of Tisdall method for determination of blood serum calcium with suggested modification. *J. Biol. Chem.* **63**:461-464, 1925.

STUDIES ON HEPATIC BILE OBTAINED FROM A PATIENT WITH AN EXTERNAL BILIARY FISTULA*

Its Composition and Changes after Diamox Administration

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RECENTLY, a patient with an external biliary fistula was admitted to the Montefiore Hospital in New York City. Since the opportunity to study hepatic bile extensively over a prolonged period rarely presents itself, it was decided to investigate the general characteristics of the bile, the electrolyte pattern, the lipid pattern and the excretion of certain heavy metals.‡ After the bile electrolyte and cholesterol concentrations had been found to vary within very narrow limits, the possible effect on the bile electrolytes of Diamox, a carbonic anhydrase inhibitor, and on the bile cholesterol of β-sitosterol by mouth was also investigated.

CASE REPORT

In January, 1954, S.G., a 73-year-old housewife, suddenly felt a colicky abdominal pain and rapidly became jaundiced. Laparotomy was performed, and multiple small common-duct gallstones, cirrhosis of the liver and ascites were found. After the stones had been removed, the jaundice was relieved, and the stools and urine were normal in color. A drain was left to the gall-bladder bed, and this came out accidentally 10 days later. Drainage of clear, yellow bile through a fistula opening in the right upper quadrant continued despite the removal of the drain. Three months later the patient was admitted to another hospital for closure of the biliary fistula. A left-sided pleural effusion was noted, and thoracentesis was performed. Cells interpreted as malignant were seen in a cell block of the pleural fluid, and operative repair of the fistula was therefore not attempted. She was transferred in June to Montefiore Hospital for further care.

She had had hypertension for many years, with increasing exertional dyspnea for the past 5 years.

Physical examination showed a pleasant and co-operative woman who weighed 55 kg. and was in no distress. Very infrequently she had fleeting episodes of disorientation, usually at night. There was no icterus or clubbing, no spider angiomas and no petechiae. There were dullness to percussion and absent breath sounds in the lower left aspect of the chest. The abdomen was protuberant, with a fluid wave, and bile was draining from an opening in the upper right quadrant. The liver edge was palpable 3 fingerbreadths below the costal margin. On pelvic and rectal examination no masses were noted.

The temperature was 98.6°F., the pulse 76, and the respirations 14. The blood pressure was 145/76.

Examination of the blood disclosed a red-cell count of 3,100,000, with a hemoglobin of 10 gm. per 100 ml., and a white-cell count of 6000, with a normal differential. The specific gravity of the urine ranged from 1.008 to 1.030. No sugar, albumin or bile was observed in the urine. Urobilinogen was present. Microscopical examination was negative. The blood sugar was 100 mg., the blood urea nitrogen 15 mg., and the thymol turbidity 8 units per 100 ml. Cephalin flocculation was negative. The alkaline phosphatase was 6.5 Bodansky units. Bromsulfalein retention was 15 per cent after 1 hour, and the prothrombin time was 15.8 seconds (control, 12.2 seconds). The serum total protein was 6.2 gm., the albumin 3.0 gm. and the globulin 3.2 gm. per 100 ml. X-ray studies confirmed the presence of a left-sided pleural effusion.

A catheter was introduced into the fistula. A catheter cholangiogram showed patency of the common bile duct; the catheter tip was in the cystic duct, near the junction of the cystic and common bile ducts. On 1 occasion a particularly heavy sediment was noted in a 24-hour collection

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‡To be reported subsequently.

of catheter bile. A cell block was made from this sediment, and cells interpreted as malignant were noted. Culture of catheter bile was negative on 2 occasions, and *Aerobacter aerogenes* and *Proteus vulgaris* were noted on a 3d occasion. When the bile was shaken little foam was seen.

Because of the reported presence of malignant cells in the pleural fluid and bile, surgical measures appeared contraindicated, and medical palliative therapy was decided upon.

With the bile draining through an indwelling catheter, the patient was comfortable. Her clinical condition, including weight, appetite and level of activity, was unchanged during the 4½-month investigation period. The pleural effusion was tapped on 1 occasion because of mild dyspnea, which was immediately relieved; 800 ml. of clear serous fluid was removed (the specific gravity of the fluid was 1.017). No tumor cells were found in a sample of this fluid. Two months after completion of the studies, she became anorectic, and lassitude and general weakness developed. Laboratory tests showed progressing hepatic insufficiency, with increasing bromsulfalein retention, increasing urinary urobilinogen and elevation of the prothrombin time. Despite supportive measures, including parenteral alimentation, the patient died in March, 1955.

On post-mortem examination no evidence of tumor was found. The diagnoses were biliary cirrhosis, choledocholithiasis, chronic fibrotic cholecystitis, and ascites. The fistula tract was lined with chronic inflammatory tissue, as was the gall-bladder bed. Although the common bile duct was only slightly dilated, the numerous small stones present were believed to have raised the intraductal pressure sufficiently to cause persistence of the external fistula. In addition, generalized arteriosclerosis, occlusion of the right coronary artery, cardiac hypertrophy and a left-sided pleural effusion (transudate) were noted.

Experimental Studies

Method

The bile was collected under oil, through a No. 14 French plastic catheter introduced to a point within 2 or 3 cm. of the junction of the cystic and common bile ducts. The catheter was connected to the collection bottle by Venopac tubing long enough so that the patient was free to move about in bed and into a wheel chair. Twenty-four-hour collections were made daily. In an attempt to estimate the fraction of the total hepatic bile volume being recovered, two tests of bromsulfalein excretion were performed. After intravenous administration of 275 mg. (5 mg. per kilogram of body weight), bile and urine were collected over twenty-four and twelve-hour periods respectively. The amount of bromsulfalein recovered in the collected bile and urine was determined by colorimetric assay by the use of the technic of Cantarow and Wirts,[1] with minor modifications. The specific gravity, pH and osmotic pressure of the bile were recorded. pH was determined immediately at the end of each twenty-four-hour period by means of a Beckman pH meter. Osmotic pressure was measured in a Fiske osmometer.

The following electrolytes were determined: sodium and potassium (flame photometer); chloride (Van Slyke and Heller method); total carbon dioxide (Van Slyke method); and calcium (Clark and Collip method on acid-ashed bile samples). Determination of bile salt concentration was attempted by the method of Peoples[2] in which the iron content of an alcoholic filtrate is colorimetrically compared with that of a standard.

All lipid fractions were measured on a Bloor (absolute alcohol, 3 parts, and anhydrous ether, 1 part) extract of serum or bile. Total lipids were determined gravimetrically,[3] lipid phosphorus by a modification of the Fiske and Subbarow[4] technic and total cholesterol by the method of Bloor and Knudson.[5] Determinations were done at varying intervals over a ninety-day period.

Table 1. *Bile Volume, Specific Gravity, pH, Osmotic Pressure and Electrolyte and Lipid Concentrations in 18 Daily Collections.*

Value	Volume of Fistula Bile	Specific Gravity	pH	Osmotic Pressure	Sodium	Potassium	Calcium	Chloride	Bicarbonate	Total Lipids	Lipid Phosphorus	Cholesterol
	ml.			*milli-osmols/liter*	*milli-equiv./liter*	*milli-equiv./liter*	*mg./100 ml.*	*milli-equiv./liter*	*milli-equiv./liter*	*mg./100 ml.*	*mg./100 ml.*	*mg./100 ml.*
Average	243	1.010	7.46	306	151	4.2	5.7	115	28	36	2.5	9
Minimum	180	1.009	7.25	299	148	4.0	5.4	114	25	27	0.38	6
Maximum	292	1.012	7.92	311	152	4.4	6.4	117	32	62	4.7	14

Results

The volume, specific gravity, pH, osmotic pressure and lipid and electrolyte concentrations are shown in Table 1. The average daily volume of catheter bile was 243 ml., with a range of 180 to 292 ml. When 275 ml. of bromsulfalein was given intravenously, 86 mg. was recovered in one twenty-four-hour collection of 185 ml., and 107 mg. in a second twenty-four-hour collection of 242 ml. On both occasions, the total urinary excretion of bromsulfalein was less than 5 mg. If all the bromsulfalein is assumed to have been excreted in the bile (as explained below in the discussion), the total bile volume, by calculation, equaled 625 ml., of which the fistula fraction comprised a third to a half.

The specific gravity of aliquots of 18 consecutive twenty-four-hour specimens was 1.009 to 1.012, of which 11 were 1.010. The bile pH ranged from 7.25 to 7.92, with an average pH of 7.46. Ten of the 18 specimens were in the pH range of 7.30 to 7.40.

The bile electrolyte values remained constant during an eighteen-day observation period and after the period of Diamox administration. As shown in Table

l the bile sodium, potassium and chloride concentrations were higher than, and carbon dioxide concentrations approximately equal to, that of the serum. The osmotic pressure of bile samples ranged from 299 to 311 milliosmols, and that of the serum from 270 to 279 milliosmols per liter.

Bile calcium concentrations were determined twice a week for four weeks. Values ranged from 5.4 to 6.4 mg. per 100 ml., with a mean value of 5.7 mg. per 100 ml. At the beginning and end of the period the serum calcium concentrations were 10.5 and 10.1 mg. per 100 ml., respectively. At this time the serum albumin was 3.0 gm., and the serum globulin 3.2 gm. per 100 ml. The concentration of bile salts was too low to be measured by the technic employed[2] although this technic permitted bile acids to be detected in concentrations as low as 0.2 gm. per 100 ml.

The concentration of the lipid fractions in both the bile and the serum did not vary appreciably during the study. On a daily fat intake of 25 gm. the serum total lipids ranged from 475 to 713 mg. per 100 ml. (200 mg.), with an average value of 634 mg., the serum lipid phosphorus from 6.4 to 8.7 mg. per 100 ml., with an average value of 7.7 mg., and the serum cholesterol from 136 to 147 mg. per 100 ml., with an average value of 142 mg. The bile total lipid, lipid phosphorus and cholesterol were all much lower than the corresponding serum values. The bile cholesterol values (6 to 14 mg. per 100 ml.) were so low as to be barely detectable by the technic used.

Effect of Diamox on Bile

Diamox effect was investigated in two twenty-four-hour trials (Table 2). In each, 1250 mg. was given orally: 500 mg. initially, followed by 250 mg. every six hours. Samples of urine and bile were collected under oil every three hours for nine hours. Bile was then collected for an additional fifteen hours, and examined as one specimen. Serum electrolyte concentrations were determined at the onset, after 2 doses and at the end of the twenty-four-hour period.

Distinctly similar changes in the electrolyte concentrations of the bile, serum and urine occurred in both trials (Table 2). After the administration of Diamox, the bile chloride concentration rose as the bicarbonate concentration fell. The bile electrolyte changes reflected those of the serum, whereas the bicarbonate concentration fell to 22 milliequiv. per liter in the first trial and to 19 milliequiv. per liter, with accompanying somnolence, in the second trial. This hyperchloremic acidosis followed a marked rise in the urinary excretion of bicarbonate and a decrease in that of chloride. Serum and bile sodium and potassium concentrations changed slightly in both trials, but these changes were within the limits of variation observed during the baseline period. After Diamox withdrawal, the bile electrolyte concentrations returned to normal as the serum electrolyte concentrations returned to normal. There was no change in the daily volume of fistula bile during either trial.

TABLE 2. *Effect of Diamox on Biliary, Serum and Urinary Electrolytes during Two Trials.*

TIME OF DETERMINATION	SODIUM			POTASSIUM		
	BILE	SERUM	URINE	BILE	SERUM	URINE
	milliequiv./liter	*milliequiv./liter*	*milliequiv./hr.*	*milliequiv./liter*	*milliequiv./liter*	*milliequiv./hr.*
Before Diamox administration	154 150	142 142	— 0.28	4.6 5.3	3.7 3.8	— 0.36
3 hr. after Diamox administration	153 150	— —	1.70 0.22	3.9 2.0	— —	1.02 0.75
6 hr. after Diamox administration	154 150	— 142	2.59 0.43	3.8 5.3	— 3.0	1.10 1.35
9 hr. after Diamox administration	152 153	144 —	3.10 1.05	4.0 5.0	3.7 —	2.10 1.85
24 hr. after Diamox administration	154 148	144 140	— —	4.2 4.8	3.7 4.1	— —

Effect of Sitosterol on Bile

The effect of β-sitosterol on the bile lipids was studied. β-sitosterol, 7.5 gm. as a 25 per cent suspension, was given orally three times daily immediately before meals. The sitosterol was given for twenty-eight days, and the lipid pattern of the bile analyzed over a five-week period before and an eight-week period after the month of sitosterol administration.

No definite effect on the bile lipids was observed. The bile cholesterol concentration rose from 8 mg. to 16 mg. and 25 mg. per 100 ml. on the last two values measured during the twenty-eight-day period. The cholesterol concentration then fell to the previous levels of 6 to 14 mg. per 100 ml. within a week of the discontinuance of sitosterol administration. No effect by sitosterol on the serum lipids was noted.

DISCUSSION

This study concerned the characteristics of the hepatic bile in a patient with an incomplete biliary fistula. When it was noted that the fistula fraction of this patient's total output was relatively constant,

an attempt was made to determine the total output by measurement of the recovery of bromsulfalein in the fistula fraction, over a twenty-four-hour period. Wirts and Cantarow[6] have shown that 67 to 100 per cent of an injected dose of bromsulfalein is normally excreted in the bile in man in two hours, with slowly decreasing amounts subsequently. If it is assumed that, even in the presence of hepatic damage, all or most of the bromsulfalein would be excreted within twenty-four hours and that the fistula drained a constant fraction of the total bile produced, the total daily bile volume in this patient was approximately 600 ml. This value was lower than the 825 ml. per day that would be expected for such a patient on the basis of Sobotka's[7] estimate of normal hepatic bile flow in man at 15 ml. per kilogram of body weight. Other estimates of daily hepatic bile volume range from 500 to 1200 ml. per day. The observation that this patient's daily volume was in higher values for sodium (averages of 174 and 183 milliequiv. per liter) and bicarbonate (averages 34 and 35 milliequiv. per liter) and lower values for chloride (averages of 64 and 84 milliequiv. per liter) than those observed for the serum. The average values compiled from the literature by Reinhold and Wilson for the serum of dogs were as follows: sodium, 118 milliequiv., bicarbonate, 22 milliequiv. and chloride, 110 milliequiv. per liter. In man, Gamble[11] indicates diagrammatically that a higher sodium, lower chloride and higher bicarbonate concentration exist in the bile than in the serum. Ravdin and his associates[12] studied human liver bile obtained in the period immediately after the release of common-duct obstruction. Total base was found to range from 121 to 181 milliequiv. per liter, with a mean value of 157 milliequiv. per liter during the first five days and 161 milliequiv. per liter during the second five days of collection. The bile chloride concentration was

TABLE 2 *(Concluded).*

TIME OF DETERMINATION	CHLORIDE			BICARBONATE			pH		
	BILE	SERUM	URINE	BILE	SERUM	URINE	BILE	SERUM	URINE
	milliequiv./liter	*milliequiv./liter*	*milliequiv./hr.*	*milliequiv./liter*	*milliequiv./liter*	*milliequiv./hr.*			
Before Diamox administration	115.0	104.0	—	26.0	26.6	—	7.40	—	6.5
	115.0	106.0	1.29	25.9	27.0	0.06	7.40	—	5.2
3 hr. after Diamox administration	121.0	—	1.07	22.0	—	1.04	7.50	—	7.1
	127.7	—	0.58	23.0	—	0.88	7.60	—	7.5
6 hr. after Diamox administration	121.0	—	0.90	22.0	—	0.96	7.32	—	7.5
	124.0	103.0	0.88	20.9	22.1	1.75	7.38	—	7.8
9 hr. after Diamox administration	121.5	110.4	1.20	27.7	25.0	2.02	7.30	—	8.5
	132.0	—	1.05	21.0	—	2.68	7.40	—	8.4
24 hr. after Diamox administration	120.0	111.0	—	25.0	22.0	—	7.30	—	—
	125.6	112.0	—	20.2	19.1	—	7.35	—	—

the low range of expected values may be explained by the daily loss of bile salts for over eight months and by general debility because of the underlying disease.

The low specific gravity of 1.010 is one of the major characteristics of hepatic, as compared to gall-bladder, bile. As tabulated by Sobotka,[7] numerous investigators have found the specific gravity of hepatic bile to be in the range of 1.010, and that of gall-bladder bile to vary from 1.026 to 1.050. The average pH of 7.46 noted in this study is in agreement with values previously observed. The pH values of bile, also tabulated by Sobotka, range from 7.1 to 8.62 for hepatic, and 5.6 to 7.0 for gall-bladder bile. An exception to this is the finding of Reinhold and Ferguson[8] of an occasional gall-bladder bile pH as high as 7.14, and common-hepatic-duct bile pH as low as 6.8, in dogs. However, in their study, as in the other investigations noted, the majority of gall-bladder specimens had a pH below 7.0, and the hepatic bile specimens one of 7.2 or above.

The ionic content of hepatic bile in dogs has been investigated by Reinhold and Wilson[9] and Ravdin et al.[10] Both groups of workers found the bile to have found to be higher than that of the plasma immediately after release of the obstruction (mean value of 111 milliequiv. per liter), but in patients who recovered, the concentration gradually fell to a mean value of 97.8 milliequiv. per liter.

In the patient described above, therefore, the chloride value in the bile (116 milliequiv. per liter) was definitely above normal. This may be explained by the low concentration of bile salts and resultant higher chloride and lower sodium concentrations in the bile, as a result of shifts to maintain electrolyte balance. As indicated previously, the small amount of bile salts present could not be measured, probably because of the continued bile loss over an eight-month period and the presence of hepatic damage, which was impeding production of bile salts. In support of this explanation for the high bile chloride, Reinhold and Wilson found, in dogs, that a decrease in the concentration of bile cholate was balanced partly by a decrease in sodium and partly by an increase in bicarbonate and chloride concentrations. These changes were reversed at times when the concentrations of bile cholate were increased. In the study by Ravdin et al.[12] cited above, patients recovering from

surgery after relief of biliary obstruction showed a gradual fall of the bile chloride at the time the concentration of bile cholate was beginning to rise, further supporting this explanation for variations in the concentration of bile chloride.

The very low bile cholesterol value in the case reported above is in agreement with the repeated finding that the concentration of cholesterol in human liver bile is well below that of cholesterol in the blood. In this patient, the exceptionally low level may be attributable to the long period on a low-fat diet, the small amount of the bile salts emptied into the gastrointestinal tract and, finally, hepatic damage, which interfered with cholesterol production. Whether or not β-sitosterol administration leads to an increase in the concentration of bile cholesterol could not be decided on the basis of this study, since the change was not large enough, and not followed long enough, to be unequivocal.

Carbonic anhydrase has been reported to be present in the rat and mouse liver by Shacter and Shimkin[13] and Ashby.[14] These authors used chemical methods of determination, based on the technic of Philpots and Philpots as modified by Keilin and Mann.[15] Although present, the enzyme concentration was low in the laboratory animals. However, Ashby also studied three samples of human liver, and found ratios of 7.8 and 13 units per gram of tissue as compared with 100 units per milliliter of whole blood. For comparison, it may be noted that values for the human kidney (6 cases analyzed by the same method) ranged from 9 to 26 units per gram of tissue as compared with 100 units per milliliter of whole blood.

In the patient described above the inhibition of carbonic anyhydrase did not directly affect the electrolyte composition of the hepatic bile. In both trials a marked carbonic anhydrase inhibition was obtained, as shown by the changes in urinary electrolyte excretion. These changes, and the resultant alterations in the serum electrolytes, are similar to those obtained by Leaf et al.[16] and other workers after the administration of Diamox. The bile electrolyte pattern, however, varied directly with that of the serum, and the changes in bicarbonate and chloride concentration were opposite in direction to those occurring in the urine.

Summary

Human hepatic bile, of which approximately 240 ml. per twenty-four hours was collected for four and a half months from a patient with an external biliary fistula, was studied for specific gravity, pH, osmotic pressure and electrolyte and lipid composition. An estimated total daily volume of 625 ml., specific gravity of 1.010, pH of 7.2 or greater, and osmotic pressure of 300 milliosmols per liter were noted. The electrolyte pattern varied within a narrow range, with the sodium and chloride concentrations higher than, and the bicarbonate and potassium equal to, that of the serum.

The effect of Diamox, a carbonic anhydrase inhibitor, on this electrolyte pattern was investigated. Increased urinary bicarbonate excretion and chloride retention occurred, with subsequent hyperchloremic acidosis. Human hepatic bile, studied in 1 patient, was a consistently alkaline fluid with a specific gravity of 1.010, osmotic pressure of 300 milliosmols per liter and an estimated daily volume of 625 ml. The electrolyte pattern was constant, differing from that of the serum in having higher sodium and chloride concentrations. The bile electrolyte concentrations were not directly affected by carbonic anhydrase inhibition. The bile lipid concentrations were much lower than those in the serum, and were unaffected by the administration of β-sitosterol for one month.

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References

1. Cantarow, A., and Wirts, C. W. Excretion of bromsulphalein in bile. *Proc. Soc. Exper. Biol. & Med.* **47**:252-254, 1941.
2. Peoples, S. A. Simplified method for determining salts in bile. *Proc. Soc. Exper. Biol. & Med.* **30**:1117-1120, 1932.
3. Sachs, B. A., Cady, P., and Ross, G. Abnormal lipid-like material and carbohydrate in sera of patients with multiple myeloma. *Am. J. Med.* **17**:662-669, 1954.
4. Fiske, C. H., and Subbarow, Y. Colorimetric determination of phosphorus. *J. Biol. Chem.* **66**:375-400, 1925.
5. Bloor, W. R., and Knudson, A. Separate determination of cholesterol and cholesterol esters in small amounts of blood. *J. Biol. Chem.* **27**:107-112, 1916.
6. Wirts, C. W., Jr., and Cantarow, A. Study of excretion of bromsulphthalein in bile. *Am. J. Digest Dis.* **9**:101-106, 1942.
7. Sobotka, H. *Physiological Chemistry of the Bile.* 202 pp. Baltimore: Wood, 1937.
8. Reinhold, J. G., and Ferguson, L. K. Reaction of human bile and its relation to gallstone formation. *J. Exper. Med.* **49**:681-694, 1929.
9. Reinhold, J. G., and Wilson, D. W. 1. Acid-base composition of hepatic bile. 2. Changes induced by injection of hydrochloric acid and inorganic salts. 3. Effects of administration of sodium taurocholate, sodium cholate and sodium dehydrocholate (decholin). *Am. J. Physiol.* **107**:378-405, 1934.
10. Ravdin, I. S., Johnston, C. G., Riegel, C., and Wright, S. I., Jr. Studies of gall-bladder functions: anion-cation content of hepatic and gall-bladder bile. *Am. J. Physiol.* **100**:317-327, 1932.
11. Gamble, J. L. *Chemical Anatomy, Physiology and Pathology of Extracellular Fluid: A lectura syllabus.* Fifth edition. 159 pp. Cambridge: Harvard University Press, 1947.
12. Ravdin, I. S., Johnston, C. G., Riegel, C., and Wright, S. I. Study of human liver bile after release of common duct obstruction. *J. Clin. Investigation* **12**: 659-672, 1933.
13. Shacter, B., and Shimkin, M. B. Carbonic anhydrase content of normal and neoplastic tissues. *J. Nat. Cancer Inst.* **9**:155-158, 1948.
14. Ashby, W. Carbonic anhydrase in mammalian tissue. *J. Biol. Chem.* **151**:521-527, 1943.
15. Keilin, D., and Mann, T. Carbonic anhydrase: purification and nature of enzyme. *Biochem. J.* **34**:1165-1176, 1940.
16. Leaf, A., Schwartz, W. B., and Relman, A. S. Oral administration of potent carbonic anhydrase inhibitor ("diamox"). 1. Changes in electrolyte and acid-base balance. *New Eng. J. Med.* **250**:759, 1954.

IDIOPATHIC SEGMENTAL INFARCTION OF THE GREATER OMENTUM

Report of Six Cases and Review of the Literature

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PRIMARY or idiopathic segmental infarction of the greater omentum is an unusual condition. A review of the literature reveals only 37 reported cases. It is not to be confused with torsion of the greater omentum, which is a fairly well established clinical entity. It is an interesting surgical condition not only because of its rarity but also because it simulates more common and more important acute surgical abdominal emergencies. There are no distinctive clinical features to help establish the diagnosis, and hence no correct preoperative diagnosis appears to have been made. Acute appendicitis and, in 3 cases, acute cholecystitis have been the usual diagnoses. In the past three years, we have had the opportunity of observing 6 cases of this condition; in 4 the clinical impression was acute cholecystitis.

CASE REPORTS

CASE 1. L.K. (St. E. H. 51-3617), a 51-year-old streetcar operator, was admitted to the hospital on December 24, 1951, complaining of constant, severe abdominal pain of 2 days' duration. It was localized to the right lower quadrant and aggravated by coughing, breathing and moving. There was no associated nausea, vomiting, diarrhea or constipation.

Physical examination revealed tenderness and spasm in the right side of the abdomen, most marked near the umbilicus. There was no rebound tenderness. Peristalsis was normal. The liver edge was palpable 3 fingerbreadths below the right costal margin. Rectal examination was negative.

The temperature was 98.6°F. The white-cell count was 6900, with 60 per cent neutrophils. Urinalysis showed 2 or 3 red cells per high-power field in the sediment.

On December 27, because of persistent abdominal pain and tenderness, the patient was operated upon under spinal anesthesia, a right subcostal incision being made. The preoperative diagnosis was acute cholecystitis. Just below the incision an area of infarcted omentum, about 2.5 cm. in diameter, was found in relation to the parietal peritoneum. This and a grossly normal appendix were resected. The gall bladder appeared normal and contained no stones. The pathological report confirmed the hemorrhagic infarction of the omentum and described a carcinoid of the appendix. The patient made an uneventful recovery and was discharged on the 10th postoperative day.

CASE 2. M.S. (C.H. 52-1483), a 56-year-old woman, was admitted to the hospital on March 8, 1952, because of abdominal pain of 1 week's duration. The pain was sudden in onset, severe, crampy and located in the right upper quadrant of the abdomen. It radiated across the upper abdomen and to the back. There was some nausea but no vomiting. She had been constipated for 5 days.

The past history revealed previous surgery for an ovarian cyst and for a cystocele. Three years before admission, she was treated medically for a bleeding duodenal ulcer.

Physical examination of the abdomen revealed marked tenderness and spasm in the right upper quadrant over a large irregular palpable mass. Peristalsis was normal.

The temperature was 100°F. The white-cell count was 7550. Urinalysis was negative.

On March 10 operation was carried out under spinal anesthesia, a right subcostal incision being made. The preoperative diagnosis was acute cholecystitis. Directly beneath the incision was a bluish-black segment of infarcted omentum measuring approximately 12 by 10 cm., adherent to the liver and to a loop of ileum and resting directly over the fundus of the gall bladder. It was dissected away from the surrounding structures, and a normal-appearing gall bladder containing no stones was exposed. The infarcted segment was removed. The pathological report confirmed acute infarction of the greater omentum. The patient made an uneventful recovery and was discharged on the 6th postoperative day.

CASE 3. F.C. (St. E. H. 52-2738), a 41-year-old accountant, was admitted to the hospital on September 16, 1952, complaining of abdominal pain of 14 hours' duration. The pain was sudden in onset, steady, moderately severe and located in the right upper quadrant. It radiated to the right flank and the right shoulder. There was associated nausea but no vomiting.

Physical examination revealed exquisite tenderness and slight spasm in the right upper quadrant of the abdomen. There was no rebound pain, and peristalsis was normal. There were no palpable masses.

The temperature was 99.8°F. The white-cell count on admission was 10,300, with 72 per cent neutrophils. A Graham test performed on the day after admission revealed a nonfunctioning gall bladder containing many small nonopaque stones.

The patient was operated upon on September 19 under general anesthesia. The preoperative diagnosis was acute cholecystitis and cholelithiasis. A narrow segment of infarcted greater omentum, about 15 cm. long, was found lying adherent to the anterior edge of the right lobe of the liver just medial to the gall bladder. There was no torsion at its base. The gall bladder was not acutely inflamed but contained many small stones. The infarct, the gall bladder and a normal-appearing appendix were removed. The pathological report confirmed these findings. The patient made an uneventful recovery and was discharged on the 10th postoperative day.

CASE 4. A.D. (St. E. H. 53-10963), a 45-year-old housewife, was admitted to the hospital on September 16, 1953, because of abdominal pain of 1 day's duration. The pain was located in the right upper quadrant and was steady, severe, knifelike and nonradiating. There was no nausea or vomiting. She had had several previous less severe episodes. In the past, she had had an appendectomy and a hysterectomy.

Physical examination revealed mild tenderness in the right upper quadrant of the abdomen. There was a suggestion of an underlying tender mass in this area. There was no spasm, and peristalsis was normal. There was no costovertebral-angle tenderness.

The temperature was 98°F. The white-cell count was 7700, with 75 per cent neutrophils. A Graham test performed on the 2d hospital day revealed a normally functioning gall bladder containing a nonopaque calculus. An electrocardiogram was normal.

Under spinal anesthesia, exploration was carried out 3 days after admission, with a preoperative diagnosis of cholecystitis and cholelithiasis. A segment of infarcted omentum measuring about 2.5 cm. in diameter was found overlying the gall bladder. The gall bladder itself contained stones but was not acutely inflamed. The area of infarction and

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the gall bladder were removed. The pathological diagnosis was infarcted omentum and chronic cholecystitis with cholelithiasis. The patient made an uneventful recovery and was discharged on the 10th postoperative day.

CASE 5. T.C. (St. E. H. 54-3096), a 13-year-old boy, was admitted to the hospital on March 12, 1954, complaining of intermittent abdominal pain of 2 days' duration. The pain was confined to both lower quadrants. No other symptoms were present.

Physical examination showed moderate tenderness and voluntary spasm in both lower quadrants and in the suprapubic area. Rebound tenderness was referred to the right lower quadrant. Peristalsis was normal.

The temperature was 98°F. The white-cell count was 10,000. Urinalysis was negative.

On March 13 operation was carried out under spinal anesthesia, a right rectus incision being used. The preoperative diagnosis was acute appendicitis. A moderate amount of amber-colored fluid was found in the pelvis. The appendix was retrocecal in location and appeared normal. Inspection of the greater omentum revealed a bluish-black area of infarction about 2.5 cm. in diameter located in the suprapubic area. This was excised, and appendectomy carried out. The pathological report confirmed hemorrhagic infarction of the omentum, with a normal appendix. The postoperative course was uneventful, and the patient was discharged on the 8th postoperative day.

CASE 6. E. H. (St. E. H. 55-2754), a 53-year-old housewife, was admitted to the hospital on March 1, 1955, because of abdominal pain of 24 hours' duration. The pain was gradual in onset, steady, increasingly severe and located along the right side of the abdomen. There was no nausea or vomiting.

Physical examination showed tenderness along the right side of the abdomen, with maximum tenderness in the right lower quadrant. There was no spasm and no rebound tenderness. There were no palpable masses. Peristalsis was normal.

The temperature was 100.4°F. The white-cell count was 8750. Urinalysis was negative.

The patient was operated upon on the day of admission under spinal anesthesia, a right rectus incision being made. The preoperative diagnosis was acute appendicitis. A moderate amount of blood-tinged fluid was found in the right gutter. Inspection of the greater omentum revealed a bluish-black area of infarction, measuring approximately 10 by 12 by 4 cm., attached to the right side of the transverse colon. This area seemed to be separated from the remainder of the greater omentum. There was no torsion at its base. The gall bladder was thin walled and contained no stones. The appendix did not appear acutely inflamed. The area of infarction was excised, and the appendix was removed. The pathological report confirmed a diagnosis of early hemorrhagic infarction of the omentum and described a normal appendix. The postoperative course was uneventful, and the patient was discharged on the 9th postoperative day.

DISCUSSION

This report is prompted by the fact that although idiopathic segmental omental infarction is an unusual condition, we have treated 6 cases in the past three years. This brings the number of published cases to 43 since Johnson[1] described what is generally considered the first authentic case. Isolated cases have appeared in the literature since that time.[2-25] The longest series, consisting of 6 cases, was reported by Pines and Rabinovitch[4] in 1940. Historical, clinical and operative details are presented in Table 1.

The clinical importance of this condition lies in its ability to simulate other acute abdominal conditions, particularly acute appendicitis and acute cholecystitis. Most of the patients have been young or middle-aged adults, although several cases have been reported in children.[15-20] Seventy per cent have occurred in males. Occasionally, a history of trauma may be established,[6] but this has been rare. The abdominal pain is usually gradual in onset, steady, moderately severe and practically always on the right side of the abdomen. Unlike the pain of appendicitis, it is usually constant in location. It occasionally radiates to the back. Symptoms are usually of twenty-four to forty-eight hours' duration. Diarrhea and constipation are unusual.

There is a characteristic disproportion between the duration and severity of the abdominal pain and the findings on physical examination. Distention is absent and peristalsis is normal. There is severe tenderness at the site of pain, usually in the right lower quadrant and occasionally in the right upper quadrant. There may or may not be spasm in the affected area. Occasionally, there is rebound tenderness, and occasionally there is a palpable mass (as in 1 of the cases reported above). Hypersensitivity of the skin of the abdominal wall overlying the involved area has been noted by some observers.[19-25] There is usually a slight elevation of temperature, and a moderate leukocytosis is common.

At operation a small amount of serosanguineous fluid is usually observed in the peritoneal cavity. The infarction practically always occurs on the right side of the greater omentum. This area of infarction, which may vary from 2.0 to 18.0 cm. in greatest diameter, measured 12 by 10 cm. in 2 of the cases presented above. Grossly, the involved segment is hemorrhagic or gangrenous, appearing dark red to purplish black. It is usually adherent to the abdominal wall or to other structures such as the liver and gall bladder. There is no twist at the base as in true torsion. Microscopical examination shows marked venous congestion, usually thrombus formation, hemorrhagic extravasation, necrosis of fat and an inflammatory reaction of varying degrees with mononuclear, polymorphonuclear and plasma cells.

Various theories have been advanced to explain this condition. Thrombosis of omental veins is one of the basic features, and thrombosis usually follows endothelial trauma. Pines and Rabinovitch[4] believe that stretching of the omental veins may lead to injury to the endothelium, with consequent thrombosis and infarction. Totten[7] suggested that the thrombosis was secondary to local injury and rupture of the thin-walled veins of the omentum after a heavy meal. Coughing, sneezing or lifting during this period may increase intra-abdominal pressure enough to cause hemorrhagic extravasation and secondary thrombosis. However, stretching and distention of omental veins are common, whereas the disease is rare. Eger and Barto[13] believe that some anatomic peculiarity of the venous drainage of the omentum predisposes to thrombus formation because of the

TABLE 1. *Clinical Findings in Cases of Idiopathic Omental Infarction.*

SOURCE	YEAR OF REPORT	AGE OF PATIENT	SEX	DURATION OF SYMPTOMS	VOMITING	TENDERNESS	WHITE-CELL COUNT	PREOPERATIVE DIAGNOSIS	SIZE OF INFARCT
		yr.		*days*					
Johnson[1]	1932	63	M	1	No	Rt. lower quadrant	15,400	Acute appendicitis, with local peritonitis	Not recorded
Hines[2]	1934	54	M	14	Yes	Left upper quadrant	10,400	Peritoneal abscess secondary to diverticulitis	Not recorded
Berger[3]	1938	53	M	1	No	Left upper quadrant	14,300	Not recorded	Not recorded
Pines & Rabinovitch[4]	1940	63	M	6	Yes	Rt. lower quadrant	12,400	Acute appendicitis	8 x 12 cm.
Bang-Dietrichsen[5]	1940	53	F	4	No	Rt. lower quadrant	10,000	Acute appendicitis	5 cm. in diameter
	1940	40	M	4	No	Rt. lower quadrant	18,000	Acute appendicitis	Not recorded
	1940	52	M	2	No	Rt. lower quadrant	13,000	Acute appendicitis	7 x 4.5 x 1.5 cm.
	1940	37	M	2	Yes	Rt. lower quadrant	9,800	Acute appendicitis	3 x 4 cm.
	1940	47	F	3	No	Rt. lower quadrant	9,000	Acute appendicitis	2 x 2 x 0.5 cm.
	1941	46	F					Acute appendicitis	——
Schottenfeld & Rubinstein[6]	1941	7	M	6	No	Rt. upper quadrant & left upper quadrant	13,000	Acute appendicitis with local peritonitis	Not recorded
Totten[7]	1942	27	M	3½	No	Rt. lower quadrant	†	Acute appendicitis	6 x 2 cm.
Durando[8]	1942	29	M	2	No	Rt. paraumbilical	15,500	Perforated duodenal ulcer or acute appendicitis with perforation	7 x 4 cm.
	1945	58	F					Acute appendicitis	
MacKenzie & Small[9]	1946	29	M	3	No	Rt. upper quadrant & rt. lower quadrant	17,620	Acute appendicitis	11 x 7 x 4 cm.
Cagney & Milroy[10]	1947	32	M	<1	Yes	Upper abdomen	†	Perforated duodenal ulcer	2.5 x 3 cm.
Joss & Pratt[11]	1948	40	F	2	N.R.	Rt. lower quadrant	13,800	Acute appendicitis	3 x 3 cm.
Harris et al.[12]	1948	49	M	1	No	Rt. lower quadrant	5,300	Acute appendicitis	2.5 x 3 cm.
		52	M	3	No	Rt. lower quadrant	8,000	Acute appendicitis	3 x 3 cm.
Eger & Barto[13]	1949	54	F	2	No	Rt. lower quadrant	(Normal)	Acute appendicitis	3 x 4 cm.
Graham & Levinson[14]	1950	63	M	1½	No	Rt. lower quadrant	11,000	Acute appendicitis	10 cm.
		34	F	2	†	Rt. lower quadrant	13,000	Acute appendicitis	6 cm. in diameter
Manfredi[15]	1950	3	F	1	No	Rt. lower quadrant	13,800	Acute appendicitis	2 x 3 cm.
Seley[16]	1951	28	M	1	Yes	Rt. lower quadrant	10,300	Acute appendicitis	7.5 cm. in diameter
Cave[17]	1952	47	M	1	No	Rt. lower quadrant	13,500	Acute appendicitis	16 x 9 cm.
Leitner et al.[18]	1952	64	M	2	No	General	11,900	?Mesenteric thrombosis; ?acute pancreatitis; ?perforated ulcer.	6 x 3 x 1 cm.
Higgins[19]	1952	41	M	2	No	Rt. upper quadrant	10,800	Acute cholecystitis	10 x 3 cm.
Catanzaro & Farley[20]	1952	10	M	4	Yes	Rt. lower quadrant	11,900	Acute appendicitis	5.5 x 3.5 cm.
		4	F	1	No	Rt. lower quadrant	11,350	Acute appendicitis	9.0 x 4.0 cm.
Hood & Geraci[21]	1953	25	M	1½	No	Rt. upper quadrant	12,300	Acute cholecystitis	3 x 3 x 2 cm.
Kerdasha[22]	1953	32	M	6	No	Rt. side	6,500	Acute appendicitis & abscess formation; ?rupture.	16 x 4 x 2 cm.
Tille[23]	1953	39	M	4	No	Rt. lower quadrant	18,800	Acute appendicitis	3 x 5 cm.
Hallstrand[24]	1954	54	F	1½	No	Rt. flank	11,050	Acute appendicitis	7.5 cm. in diameter
		11	M	1	No	Paraumbilical	11,550	Acute appendicitis	Not recorded
		52	M	1	No	Rt. lower quadrant	10,300	Acute appendicitis	5 x 5 cm.
		3	F	4	Yes	Rt. lower quadrant	11,200	Acute appendicitis	(Large mass)
Bauman & Hoffert[25]	1954	31	M	3	No	Rt. upper quadrant	10,900	Acute cholecystitis	7.5 x 5.0 cm.
Present series	1955	51	M	2	No	Rt. lower quadrant	6,900	Acute cholecystitis	2.5 cm. in diameter
		56	F	7	No	Rt. upper quadrant	7,550	Acute cholecystitis	12 x 10 cm.
		41	M	<1*	No	Rt. upper quadrant	10,300	Acute cholecystitis	15 cm. long
		45	F	1	No	Rt. upper quadrant	7,700	Acute cholecystitis	2.5 cm. in diameter
		13	M	2	No	Rt. lower quadrant	10,000	Acute appendicitis	2.5 cm. in diameter
		53	F	1	No	Rt. lower quadrant	8,750	Acute appendicitis	12 x 10 cm.

*14 hr.
†Not recorded.

almost constant location of the infarct in the right lower portion of the omentum. Harris, Diller and Marcus[12] contend that obese, hypersthenic persons are more likely to suffer omental infarction because of increased gravitational pull of an extremely fatty omentum, resulting in rupture of a vessel. Schottenfeld and Rubinstein[6] stressed the importance of blunt trauma as an etiologic factor in this condition.

In reviewing the previously reported cases and our own, we are impressed by the lack of common etiologic factors. Conclusive evidence to support any of the theories of etiology is wanting. Many cases occurred without relation to meals, increased intra-abdominal tension or trauma. Infarcts have developed in patients of various sizes and in various parts of the greater omentum.

It appears that more experience with this condition will be necessary before adequate criteria for diagnosis can be established. This entity should be considered in the differential diagnosis of the acute abdominal emergency. A practical point, which we have derived from our experience, is the necessity for careful examination of the greater omentum for evidence of infarction in all cases in which the findings are not consistent with the clinical impression. We believe that such an examination cannot be thoroughly carried out through a McBurney incision, and it has been stated[11] that this type of incision may have contributed to the small number of cases in the literature.

The treatment of this condition is resection of the infarcted area to prevent possible complications of gangrene and adhesions. Bauman and Hoffert[25] point out that some cases of unexplained intestinal obstruction may be due to previously unrecognized omental infarcts that have become adherent to small bowel. It is noteworthy, however, that in a few cases recovery followed even though the infarcted area was not removed because of either its central location or some technical difficulty.

Summary and Conclusions

Six cases of idiopathic segmental infarction of the greater omentum are reported; 4 simulated acute cholecystitis.

Idiopathic omental infarction should be considered in the differential diagnosis of the acute abdomen.

The greater omentum should be carefully explored in all cases in which the pathological findings are not consistent with the clinical impression.

A review of 37 previously reported cases and a discussion of the findings, etiology and treatment are presented.

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References

1. Johnson, A. H. Great omentum and omental thrombosis. *Northwest Med.* **31**:285-290, 1932.
2. Hines, L. E. Hemorrhagic infarction of greater omentum. *Illinois M. J.* **66**:166, 1934.
3. Berger, A. R. Hemorrhagic infarction of greater omentum. *Arch. Surg.* **36**:497-499, 1938.
4. Pines, B., and Rabinovitch, J. Idiopathic segmental infarction of greater omentum. *Surg., Gynec. & Obst.* **71**:80-85, 1940.
5. Bain-Dietrichson, O. Tilfeulle AV infarkt: omentum majus. *Nord. Med. (Norsk mag. f. laegevidensk.)* **12**:3413, 1941.
6. Schottenfeld, L. E., and Rubinstein, H. Hemorrhage and thrombosis of omentum: their etiology in acute abdomen. *Am. J. Surg.* **51**:449-451, 1941.
7. Totten, H. P. Primary idiopathic segmental infarction of greater omentum. *Am. J. Surg.* **56**:676-679, 1942.
8. Durando, A. C. Primary infarct of greater omentum. *Bol. Soc. de cir. de Rosario* **12**:175-182, 1945.
9. MacKenzie, W. C., and Small, J. Primary idiopathic segmental infarction of greater omentum. *Canad. M. A. J.* **55**:144, 1946.
10. Cagney, M. S., and Milroy, G. Idiopathic infarction of omentum. *Brit. J. Surg.* **33**:95-97, 1947.
11. Joss, C. S., and Pratt, J. H. Primary idiopathic segmental infarction of greater omentum. *Minnesota Med.* **31**:996-999, 1948.
12. Harris, F. I., Diller, T., and Marcus, S. A. Hemorrhagic infarction of greater omentum simulating acute appendicitis: report of 2 cases. *Surgery* **23**:206-210, 1948.
13. Eger, S. A., and Barto, R. E., Jr. Primary idiopathic segmental infarction of greater omentum. *Am. J. Surg.* **78**:518, 1949.
14. Graham, J. A., and Levinson, S. A. Omental apoplexy: idiopathic segmental infarction of greater omentum. *Am. J. Digest. Dis.* **17**:114-117, 1950.
15. Manfredi, D. H. Omental segmental infarction in infancy: report of case. *Arch. Pediat.* **67**:247-249, 1950.
16. Seley, G. P. Primary idiopathic segmental hemorrhagic infarction of greater omentum. *J. Mt. Sinai Hosp.* **17**:523-525, 1951.
17. Cave, W. H. Primary idiopathic infarction of greater omentum. *Illinois M. J.* **102**:130, 1952.
18. Leitner, M. J., Jordan, C. G., Spinner, M. H., and Reese, E. C. Torsion, infarction and hemorrhage of omentum as cause of acute abdominal distress. *Ann. Surg.* **135**:103-110, 1952.
19. Higgins, G. A. Idiopathic spontaneous segmental infarction of omentum. *Arch. Surg.* **64**:395-398, 1952.
20. Catanzaro, F. P., and Farley, J. E., Jr. Omental segmental infarction: 2 cases in children. *J. Pediat.* **40**:240-242, 1952.
21. Hood, R. T., Jr., and Geraci, J. E. Infarction of omentum simulating acute cholecystitis: report of case. *Proc. Staff Meet., Mayo Clin.* **28**:296-298, 1953.
22. Kerdasha, R. Idiopathic spontaneous segmental infarction of greater omentum. *Ann. Surg.* **137**:419-423, 1953.
23. Tille, R. J., Jr. Idiopathic segmental hemorrhagic infarction of greater omentum. *Ann. Surg.* **138**:279-284, 1953.
24. Hallstrand, D. E. Primary omental infarction. *Am. J. Surg.* **87**:563-566, 1954.
25. Bauman, A., and Hoffert, P. W. Idiopathic infarction of omentum: report of 2 cases. *Ann. Int. Med.* **41**:342-349, 1954.

SPECIAL ARTICLE

MEDICAL ASPECTS OF THE WORCESTER TORNADO DISASTER

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IN the late afternoon of June 9, 1953, a tornado unexpectedly struck a section of Worcester County, Massachusetts, and in about twenty minutes created a major disaster. The problems that arose as a result of this storm were, of course, innumerable, but those that concerned the evacuation of the injured, their distribution to the various hospitals in the area and the management and care of the casualties once they arrived at the hospitals are of great importance, particularly in the planning and preparations for such disasters in the future. Although this report is presented primarily as a review of the various types of injuries and their treatment, the more important phases of evacuation and distribution of the casualties are discussed, and recommendations made for a more efficient action in the future.

The tornado struck at about 5:10 p.m. without warning and devastated a section of Worcester County that was partly residential and partly industrial. Large factories and brick buildings, as well as small houses, were ripped apart and blown like leaves before the storm. Trees were uprooted, and débris of all kinds blocked the streets in the half-mile-wide path taken by the storm across the city. In a few minutes a peaceful community was turned into chaos. The streets leading to the area were soon crowded with automobiles. Some were those of sight-seers, but most were civilian cars, ambulances and police cars, all carrying the injured to nearby hospitals. In spite of this congested traffic, practically all the casualties were evacuated within two hours. Routes to the devastated area were later guarded by police so that sight-seers were kept from the area. Earlier traffic control would have greatly facilitated evacuation of the injured.

COMMUNICATIONS

Owing to difficulties in communication, the deputy director of the Medical Division was notified belatedly of the disaster by the local Civil Defense headquarters. A check by him showed that the section chiefs of the Medical Division were already at their respective hospitals, having been summoned earlier by telephone or by broadcasts from the local radio stations. A reconnaissance of the stricken area was made by automobile, and it was immediately evident that all the persons known to be seriously injured, and the majority of those with minor injuries, had already been transferred to hospitals by ambulance or private cars. It appeared unnecessary, therefore, to establish either first-aid or evacuation stations in the area. Two physicians and two ambulances were assigned to the damaged area on stand-by duty until further rescue efforts established that no injured, dead or alive, remained. A first-aid station was established at Civil Defense headquarters, where minor injuries were treated as ambulatory cases. Such cases were few since the majority went to the nearby hospitals in the area.

One of the hospitals nearest the path of the storm was soon overcrowded by the large number of injured, but once the police became aware of this situation, cars bearing casualties were referred to other hospitals. Earlier radio communication between the police, the central Civil Defense Director's office and the hospitals would have permitted more prompt reporting of the extent of the damage and estimates of the number of casualties, as well as the earlier proper routing of casualties by the police. Hospital authorities could thereby have been informed at once of the number of casualties to be expected, and preparations could have been started without delay. Furthermore, the casualty load could have been distributed more evenly among the various hospitals with less loss of time.

Because there was no warning of the storm, which swept through the County and caused its damage within a period of about twenty minutes at a time when most physicians were at their offices, few doctors had any knowledge of the devastation caused by it. Although the telephone operators at the various hospitals notified the staff members as promptly as possible, many of the injured had already been taken to the hospitals by the time the doctors could reach their hospitals through the congested traffic. There was, therefore, temporary overcrowding and congestion in the receiving areas of the hospitals nearest the scene. Physicians who happened to be at the various hospitals at the time of the storm started at once with the aid of house officers and nurses in the triage of the casualties and treatment of the severely injured. As other doctors arrived, areas that had

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previously been designated for the treatment of certain types of injuries were adequately manned. Patients requiring hospitalization were then sent to one of these areas for treatment, depending on the injury. The necessarily irregular arrival of medical personnel assigned according to a previously established disaster plan made early modification of these plans imperative.

It is the opinion of representatives of the staffs of the five hospitals involved* that the problems confronting the civilian hospitals in the handling and treatment of mass casualties after a local disaster are unique and are not strictly comparable to those under wartime conditions. Even so, the majority of wounds were treated as they would have been under normal conditions, since the hospitals and personnel were not in the path of the storm, and since the number of casualties did not overburden the hospital facilities and the number of physicians available. It is recognized, however, that if the major hospitals and many of the doctors in the area of the disaster had been incapacitated so as to necessitate establishment of emergency first-aid stations, and later transportation of the casualties to other centers for definitive treatment or follow-up care, the wisdom of following the principles of treatment generally adopted under wartime conditions would have been unquestioned.

Records

It is important during the early hours of the disaster as well as the following days that accurate notes be kept. This is greatly facilitated by the use of volunteer stenographers, who are able to take shorthand notes during rounds and dressings. These notes not only are of great value in the day-to-day management of the patients but also constitute a permanent record. Teams of the staff doctors were formed. Each team consisted of a general surgeon, an orthopedist and an internist. This group made rounds together and saw each patient daily. The stenographers accompanied the team on its rounds so that the initial findings and progress notes could be quickly recorded on each record. This plan, which permitted a co-ordinated effort in the treatment of these patients, many of whom had multiple types of injuries, proved to be quite satisfactory.

After the patients were discharged from the hospital, they were followed in the outpatient department. In this way the final results regarding wound healing and the functional result of the treatment could be assessed.

Triage

The following methods were generally used at the five hospitals in this area in the processing of the injured. As casualties arrived at the receiving wards it became apparent at once that police control of the cars bearing the injured was essential. By the maintenance of orderly traffic the casualties could be properly examined and tagged by those handling the triage. They were then routed to the designated hospital areas, depending on the type of injury.

Some of the casualties exhibited extensive, deep abrasions owing to a sand-blast effect of dirt and débris striking at high wind velocity. The clothing in such cases was torn off by the force of the blast. In a few the particles of dirt penetrated the skin deep enough to give a tattoo effect. Fortunately, the majority of the abrasions and lacerations were small and superficial, extending only a short distance into the subcutaneous tissue. Many of the wounds were caused by flying objects of relatively low velocity and, therefore, did not penetrate deeply. Although some of the larger wounds were made by heavy flying objects, the majority were caused by falling beams, metal and other débris when victims were trapped in collapsing buildings or automobiles.

Classification

Although the majority of the patients had multiple injuries, at the time of triage they were classified according to the major injury and were sent to the hospital area designated for the treatment of that type of injury. Cases, therefore, were divided into the following groups: contusions, abrasions, and superficial lacerations not extending through the skin; shock without wounds; minor wounds extending through the skin, major wounds with or without shock; orthopedic cases; neurosurgical cases; and miscellaneous injuries, including chest and abdominal injuries.

Emergency Therapy

The many people who sustained only minor injuries, abrasions and contusions were segregated and treated later. The initial efforts in treatment were directed toward the injured who were either in shock or who had major injuries and in whom the prevention of shock was important. In such cases intravenous infusions of fluids, such as physiologic saline solution, plasma and plasma expanders were used. Shock in some of the injured was in part due to blood loss; transfusions were started as soon as possible in these cases. When the patients began to respond to therapy, they were taken to the surgery for definitive treatment.

Blood for transfusions was in plentiful supply since many relatives and friends of the injured, and others wishing to contribute something to the effort, volunteered in large numbers as donors. There was no shortage of technicians to draw and process all the blood that was needed since most of the hospitals in the area had auxiliary personnel trained in the technics of typing and bleeding donors under the

*Worcester City, Memorial, Holden District, St. Vincent and Hahnemann hospitals.

Civil Defense program. In fact, after a generous supply of blood had been drawn, many persons anxious to donate were turned away. The response of the people in the time of need was therefore most gratifying.

Soft-Tissue Wounds

Casualties with soft-tissue wounds, whether occurring as a major injury or in conjunction with fractures or neurosurgical injuries, constitute the cases in which treatment is most controversial. Therefore, the records of this group of inpatients at the five hospitals in the area treating the casualties have been reviewed, and the results of treatment tabulated. The records of those treated in the outpatient department were not reviewed since the follow-up records were considered unsatisfactory. Table 1 shows the combined experience of these hospitals in the treatment of soft-tissue wounds *not* complicated by fractures or neurosurgical injuries.

The frequency of infection in primarily closed wounds varied in the different hospitals from 5.2 per cent to 12 per cent, with an over-all average of 10.5 per cent. This is not considered abnormally high and is comparable to the results in the treatment of contaminated wounds in many hospital emergency wards.

Table 2 presents the results when wounds of patients admitted to the hospitals were either closed secondarily or left open.

Table 1. *Treatment of Hospital Inpatients with Uncomplicated Injuries.*

Treatment	No. of Wounds	No. of Clean Wounds	No. of Infections
Primary closure	133	119	14 (10.5%)
Secondary closure	22	20	2 (9.1%)
Open	26	23	3 (11.5%)
Totals	181	162	19 (10.5%)

It is of interest that the percentages of infections in the group closed primarily and those either closed secondarily or left open were almost identical. This indicates that when the medical facilities are not unduly taxed, infection is no more frequent when wounds are treated by primary closure than when they are dealt with by the delayed closure or open method.

Little has been written about the management of soft-tissue wounds in civilian disasters. We therefore believe that an analysis of the management of the soft-tissue wounds in this disaster offers an excellent opportunity to evaluate varying methods of treatment.

Should the dictum laid down in World War II — namely, the treatment of wounds by the open method — be applied without exception to every civilian disaster? If so, unnecessarily long periods of hospitalization and medical care would probably result. It should again be emphasized that the conditions surrounding this disaster were different from those in a wartime environment. The casualties all occurred during one period of violence that was of short duration and not repeated. Although there was some congestion of traffic during the first hour after the storm had struck, most of the casualties had been taken to one of the five hospitals in the area within two hours, and within a short time thereafter were ready for definitive treatment. The majority of the injured, therefore, were treated within three or four hours of the tornado. This is a period well in advance of the deadline of six to eight hours when bacterial contamination becomes invasive. Also within an hour or two of the storm, surgical personnel capable of carrying out definitive treatment of the wounds were present in adequate numbers in all the hospitals. In addition, many surgeons from nearby cities volunteered their services, but few were needed. Hence, within a short time, these hospitals were operating on a well organized plan that permitted each casualty to be treated as usual under civilian conditions. It seemed logical, therefore, that each wound should be treated as in civilian practice instead of strict adherence to the wartime open method of treatment for all cases.

Table 2. *Frequency of Infection.*

Treatment	No. of Cases	No. of Cases with Infection
Secondary closure or left open	48	5 (10.4%)

It is generally agreed that the ideal treatment of a wound of soft tissue is débridement and primary suture, if the wound can be treated before active invasion of contaminating bacteria has begun. Such treatment ensures a short convalescence and superior results as far as cosmetic appearance of the scar and late wound complications are concerned. There is, or course, the risk of infection. Under ideal civilian circumstances this risk is slight and, with modern surgical facilities, does not outweigh the advantages of débridement and primary closure. On the other hand wounds incurred under the conditions of large-scale disaster, such as warfare, delayed and secondary closure of soft-tissue wounds, after a thorough and careful débridement, is insisted upon. Since the necessary factors of thorough débridement and close observation by experienced surgeons cannot be guaranteed under wartime conditions long-disabling and even fatal complications are frequent enough to make primary closure under such circumstances unnecessary and dangerous. Strict interdiction against débridement and primary closure of soft-tissue wounds in the last war was accordingly accepted as a wise policy.

In line with this conclusion the general policy in one of the larger hospitals was to treat the wounds as they would ordinarily have been treated under normal conditions. The majority, therefore, were débrided and closed. In several of the other hospitals some of the wounds were closed, others were treated by delayed closure, and still others were left open. The results in the hospital where the majority of the wounds were closed after thorough débridement were found to be a little better than those obtained in several of the other hospitals where some of the wounds were either closed secondarily or were left open. Nevertheless, it is apparent and generally agreed that heavily contaminated wounds, in which a thorough débridement is difficult or impossible because of the presence of vital structures, should not be closed primarily. On the other hand, it is our belief that if a soft-tissue wound can be carefully and thoroughly débrided within a few hours of injury, it can be closed primarily, thereby minimizing the period of disability and producing a minimal scar. As previously stated, to adopt such a plan implies that the number of casualties is not excessive and that the medical facilities are such that the injured can be treated promptly and carefully.

TABLE 3. *Treatment of Complicated Wounds in All Five Hospitals.*

TYPE OF INJURY	NO. OF WOUNDS	NO. OF CLEAN WOUNDS	NO. OF INFECTIONS
Orthopedic with lacerations:			
Treated with primary closure	54	46	8 (14.8%)
Treated with secondary closure	4	2	2 (50.0%)
Open treatment	15	14	1 (6.6%)
Neurosurgical with lacerations:			
Treated with primary closure	48	44	4 (8.3%)
Treated with secondary closure	0	0	0 (—)
Open treatment	1	1	0 (—)
Combined orthopedic & neurosurgical:			
Treated with primary closure	26	20	6 (23.0%)
Treated with secondary closure	4	4	0 (—)
Open treatment	8	7	1 (12.5%)

ORTHOPEDIC AND NEUROSURGICAL INJURIES

The general principles applicable to the handling of soft-tissue wounds might well be the basis for the management of orthopedic and neurosurgical injuries. Rarely is there an indication for heroic measures in the immediate treatment of fractures, and there is a well deserved place for a maturely conservative attitude when one is faced with a large number of fracture patients at one time. In general the anticipation or treatment of shock, adequate temporary immobilization and institution of proper prophylactic antibiotics will constitute satisfactory immediate care and will permit carefully planned, definitive treatment under optimum conditions. This group comprises the more seriously wounded patients, who are often in poorer general condition. It is axiomatic that in this group serious consideration should be given to the open treatment of compound fractures, particularly when there is considerable fragmentation of the bones or extensive contamination of the wound.

Table 3 records the experience of the five hospitals in the treatment of complicated wounds. It is apparent that infection is more frequent in wounds that have accompanying orthopedic or neurosurgical complications.

In the treatment of compound fractures, it is highly desirable to achieve a condition in the wound that will allow closure of the skin. This means thorough débridement, with removal of bone fragments separated from periosteum and foreign bodies. At times actual wound excision may be desirable if important structures are not sacrificed. There may be situations in which severely contused, large wounds cannot be adequately débrided or excised. These wounds must be left open, and proper local and systemic treatment instituted. Such wounds should compel the continuous consideration of possible gas-bacillus or tetanus infection.

Again, the same principles should apply to neurosurgical injuries, which were quite common in this disaster. There were many kinds, and they were often associated with injuries to the chest and to the extremities. Certain impressions regarding the management of these injuries were gained. The neurosurgeon should, at the outset, be freely available so that he may triage the neurosurgically injured and also consult freely with other surgeons on patients with multiple injuries. It is obvious that he cannot engage in any form of craniotomy at this period. Patients with compound skull injuries should have an early baseline neurologic examination and temporary dressings and thereafter careful observations of the vital signs. Those with serious closed head injuries should also have a brief but informative baseline neurologic examination and should then be observed carefully. Attention should be paid to the maintenance of an adequate airway, and changes in the neurologic and vital signs should be carefully noted. Scalp lacerations alone, or in association with mild concussion, should be seen by the neurosurgeon, and then assigned to members of the house staff or the general surgical staff for closure. In general these wounds, whether simple or compound, after a satisfactory cleansing and débridement, should be closed primarily as soon as possible. After such disposition the neurosurgeon can then undertake to care for the compound skull fractures. This may take a long time.

Chest Injuries

Several of the casualties had chest injuries of an unusual pattern. They presented the usual picture of blast injuries to the lungs characterized by interstitial hemorrhage and edema, with or without pneumothorax, hemothorax and visceral pleural tears such as have been repeatedly reported as the result of war injuries. In the latter group the victim has been subjected to stresses of air pressure generated by close proximity to high explosives. Although this has been the common cause of such injury, the same effect can apparently be achieved by nature, when the pressure of the atmosphere is changed sufficiently and rapidly enough. These conditions were apparently met in one small area in Holden and several smaller scattered areas in Worcester. In Holden, where several cases were found, all occurred within a small geographic area in the center of the storm path where it is assumed that the changes in pressure were greatest. These patients exhibited in common certain features, which were subject to variation in intensity according to the severity of the injury or to pre-existing complications such as bronchial asthma. All appeared anxious and excited. Respirations were rapid, with labored and forced inspiration and expiration. The pulse was rapid, blood pressure low, abdominal muscles set, and the need for oxygen apparent. Subcutaneous emphysema, hemoptysis and pain were less common.

These patients were treated with bed rest in the nearly upright position. Oxygen and analgesics were used as indicated and serial x-ray examinations of the chest were made to determine the extent of the hemothorax, pneumothorax and pulmonary edema. In 2 cases of pneumothorax the lungs were so compressed as to require constant suction of the pleural cavity. This resulted in immediate relief in each case. All these casualties recovered without after-effects.

Conclusions

In view of the results from the treatment of a large number of wounds resulting from a major civilian catastrophe under the conditions described above, certain conclusions can be drawn. When the medical facilities are adequate to care for the number of casualties involved, major wounds that are not accompanied by unusual devitalization and contamination and can be carefully débrided may be safely closed primarily. These wounds under civilian conditions can be watched from day to day and usually by the operating surgeon. If active infection supervenes, it can be detected early and appropriately and energetically treated. In this way there is a great saving in patient days, and the resultant scar is usually better than the one that results when the wound is closed secondarily or left open. Other major wounds with extensive tissue devitalization or with numerous foreign bodies that cannot be completely removed should be débrided as much as possible and then closed secondarily or left open, depending on the situation.

An established plan of co-ordinated action between police, central office of Civilian Defense and the various hospitals, with radio communications between these three services, would greatly facilitate the evacuation and distribution of the injured in time of disaster.

Police help is essential to control traffic in the disaster area and also at the receiving wards of the various hospitals so that prompt transportation of the injured and their triage can be carried out efficiently.

Each hospital should have its own carefully thought out and organized disaster plan. Teams formed from the staff personnel should be assigned to treat the various types of injured in previously designated hospital areas.

MEDICAL PROGRESS

THORACIC SURGERY

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THE three years that have elapsed since the last progress report on thoracic surgery appeared in this journal have been a time of consolidation of past gains rather than of breaking new ground. Certainly this has been true so far as diseases of the lung are concerned. In the cardiovascular field considerable advance has been made.

An example of such an advance is the changing attitude toward aneurysm of the thoracic aorta. Three years ago symptomatic therapy of thoracic aneurysms was accepted as the useful, if not ideal, method of management. Intrasaccular wiring had been shown to relieve pain in a high proportion of cases and could be carried out with a reasonable mortality.[1] Wrapping of aneurysms with cellophane and other sclerosing agents was also employed, with

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mediocre success. In 1953, however, Bahnson[2,3] demonstrated that excision of saccular aneurysms with lateral suture of the thoracic aorta was feasible and advocated this as the definitive treatment of syphilitic aneurysms of that structure. He pointed out that the chief limiting factor was danger to the cerebral vessels, and here it is that the employment of temporary shunts to protect the cerebral circulation and the use of hypothermia should prove valuable.[4-6]

The radical treatment of aortic aneurysms has not been limited to syphilitic forms of the disease. DeBakey and Cooley[7] have extended their experience with the abdominal aorta to the thorax and demonstrated the feasibility of resection and replacement by homograft of the thoracic aorta in arteriosclerotic aneurysms. Here, again, results are generally excellent unless cerebral vessels are involved. Such radical attacks on degenerative lesions can, of course, only be considered curative so far as the local lesion is concerned. When such a lesion is a manifestation of injury — and traumatic aneurysms of the thoracic aorta have been described[8] — excision, with or without graft, is a definitive procedure.

Lung

Anatomy and Physiology

This last year has seen the publication in book form of Boyden's[9] exhaustive studies on the segmental anatomy of the lung. The greatest deficiency in present knowledge of the gross anatomy of the lung is the lack of a precise description of the lymphatic drainage of the various segments. No authoritative anatomic study of this subject has appeared since that of Rouvière[10] in 1938. It may be that no more descriptive study is possible since the pulmonary lymphatic system is essentially that of a network although the main channels, as Rouvière has shown, can be identified. Attempts to map these by the use of various radioactive colloids and vital dyes have been interesting, but the practical difficulties of systematic studies of this kind in human beings are enormous.[11-13]

A fresh slant on the functional anatomy of the lung has recently been presented by Churchill,[14] who points out that extensive obliteration of the finer air passages is common but that, despite this, the alveoli normally served by these passages remain air filled, for air enters by way of collateral air drift. The bronchial-artery circulation to such areas is increased to produce a physiologic blockade against the shunting of venous blood across air-containing but inefficiently ventilated lung. The diseased portion of the lung therefore remains an air-containing space filler to prevent compensatory emphysema of normal lung. This is the architectural design of the lung.

The space-filling function of the lung is generally considered subordinate to its respiratory function. Comroe[15] has recently edited an excellent general review of the clinical physiology of the lung and the application of pulmonary-function tests. It is quite evident that physiologic tests indicate only how disease has altered function—they do not make an anatomic, bacteriologic or pathologic diagnosis. Within certain limits they can be considered quantitative, particularly if used in serial fashion in a given patient. Woodruff, Merkel and Wright[16] have discussed the clinical usefulness of function tests and their influence on decisions in thoracic surgery. They emphasize again the importance of the chest wall in preserving the ventilatory function of the lungs. Gaensler et al.[17] report an extensive program of screening studies of pulmonary function before operation in 460 patients with advanced pulmonary tuberculosis. They conclude that although access to objective data concerning pulmonary function at the time operative decisions were made did not eliminate postoperative invalidism and deaths, an unfortunate outcome after surgery occurred most often when pleas of patient, relatives and physicians prevailed over objective data from the laboratory. Björk,[18] who has written prolifically on the subject, apparently agrees, though he admits, "the best of all pulmonary function tests is the operation itself."

It is only recently that attention has been paid, in the surgical literature at least, to the importance of pulmonary hypertension as an indication of marginal pulmonary reserve. Adams et al.[19] have discussed this aspect of surgical risk and demonstrated, in the laboratory animal, the wide margin of safety in the normal lung but the danger of encroaching further on the lesser circulation when some degree of pulmonary hypertension is present. It is surprising, perhaps, that cardiac catheterization has not been more widely used as a "function test" in evaluating the borderline risk. In 1951, Carlens, Hanson and Nordenström[20] showed that it was safe to occlude the pulmonary artery to one lung in the unanesthetized patient by the inflation of an intra-arterial balloon attached to the end of a double-lumen cardiac catheter. Sloan et al.[21] have applied this clinically in the preoperative evaluation of thoracic patients. A marked rise in pulmonary-artery pressure, an increase in arteriovenous oxygen difference and a failure to increase cardiac output were interpreted to mean impaired cardiovascular function. Of 18 patients studied, 2 patients died postoperatively of cardiorespiratory insufficiency. Both showed impaired cardiovascular function by test. No patient with normal hemodynamics died in respiratory failure. Unfortunately, the authors do not state how many with abnormal findings weathered operation successfully. Somewhat similar studies, with bronchial in addition to pulmonary-artery occlusion, have been reported by Nemir and his associates[22] from Philadelphia. A possible objection to the method is that the pressure measured is that immediately proximal to the occluding balloon. Under these circumstances rises in pressure of only a few millimeters of mercury must be interpreted with caution.

The autonomic control of pulmonary function, particularly the influence of sympathetic and parasympathetic nerves upon the pulmonary vessels, is poorly defined. Such clinical studies as do exist are hampered by difficulties in classification and definition of emphysema and the asthmatic state. Without any widespread agreement regarding the nature of the pathologic and physiologic processes involved, it is impossible to measure one clinical series against another. The few studies that are available on the effect of vagus section in lowering pulmonary-artery pressure are open to the criticism that only relatively minor changes in pressure have been recorded and no measurements of cardiac output — such as volume flow — are reported.[23,24]

In passing it should be pointed out that the value of resection of localized emphysema when it assumes great size, and may encroach upon functional lung, is well established. Perhaps the most interesting and dramatic form of this disease occurs in infants and children.[25,26]

Bronchiectasis

An excellent summary of the present situation concerning bronchiectasis is contained in a recent editorial in the *Lancet*.[27] It is clearly apparent that preantibiotic series, such as the classic one of Perry and King,[28] were heavily weighted by severe cases, for as a general rule only severe cases were put through the extensive diagnostic procedures needed to establish the diagnosis. Valid as the early series were for drawing conclusions about the natural history of severe bronchiectasis, they are of limited value for prognosis at present when severe, localized, saccular bronchiectasis is becoming less common. It is clear now that operation is relatively safe, so far as mortality and postoperative septic complications are concerned. The real drawback is the relatively high incidence of unsatisfactory end results if these are judged by a third party.[29] As the editorial points out, "A surgeon's estimate of his own results is liable to be unconsciously influenced not only by his own enthusiasm but also by the natural wish of many patients to gratify one who has made strenuous and dramatic efforts to relieve them." It seems likely that the majority of bad end results of operation for bronchiectasis, excluding patients with hopelessly advanced disease, are to be found among those in whom there is a large element of diffuse bronchitis and in whom, perhaps, the area resected represented only a more accentuated site of a diffuse disease. The sensible thing to do, therefore, would be to reserve surgery for specific, easily defined, objectives — namely, localized disease, profuse cough and sputum, repeated pneumonia (recurring in the same site) and hemorrhage. In addition, one might mention empyema, which is often the manifestation of a serious underlying local pathologic process.

Bilateral segmental resection at one operation has been proposed, and its feasibility demonstrated.[30] Under exceptional circumstances it appears possibly justified, the risk of bilateral chest complications being balanced against the advantage of ridding the patient of productive septic foci during his postoperative period. Such a balance requires acute clinical judgment. In addition, it must be admitted that a bilateral program is often abandoned when it is found that removal of disease on one side provides such clinical relief of symptoms that a second operation is not judged necessary. The long-term results of bilateral-resection programs, though occasionally dramatic, can only be considered a qualified success.[31-33]

A great deal has been written about the use of water-soluble iodine compounds to replace lipiodol as a bronchographic agent to overcome the disadvantage that if it is not promptly cleared by coughing, — which, incidentally, it usually is unless emphysema is present, — subsequent interpretation of parenchymal shadows is dangerously confused. A number of water-soluble agents have been employed and found useful.[34,35] In general, the radiopaque agent is Diodrast incorporated in a carrier such as methyl-cellulose to provide viscosity. Usually, absorption of the radiopaque medium is extremely rapid — so much so that it may be difficult to obtain satisfactory films with the proper degree of contrast. There appears also to be a certain incidence of sensitivity to the carrier agents employed, and local inflammatory complications have been reported.[36] Recently, absorbable agents in an oily, nonabsorbable base have been advocated and have proved useful. There is no question that, in certain circumstances, absorbable agents will have distinct advantages, but that lipiodol and related compounds cannot yet be considered obsolete.

Closely allied to the problem of bronchiectasis is the subject of chronic interstitial pneumonitis, often confused wtih bronchiectasis as well as carcinoma. Waddell, Sniffen and Whytehead[37] have shed some light on the pathogenesis of this condition when it is associated with cholesterol deposition or so-called "cholesterol pneumonitis." Using rabbits, these authors produced the pathologic picture of the disease by rendering the animals lipemic and then inducing certain chronic pulmonary infections. Cholesterol deposited in the tissues is removed with difficulty. The authors postulate a profound change in the physicochemical milieu as part of the reaction to infection or injury — for example, local change in tissue pH — that might well lead to cracking of an emulsion or similar changes in a colloidal system. The clinical implications of this study, such as the effect of diet in the treatment of the pulmonary invalid, are intriguing.

Tumors

Cancer of the lung continues to be an important problem in thoracic surgery. A number of excellent reports published in the past few years,[38-40] added to previous reports, define the status of resection for

this disease. Invariably, the percentage of patients judged to be candidates for resection is lower than might be wished—usually about 50 per cent. In general an over five-year survival of 20 to 25 per cent in the resected cases is standard, making the total five-year salvage in any large series of cases approximately 10 per cent or less. As has been pointed out frequently, five-year survival is only one standard by which the surgical treatment of cancer is measured, and not necessarily the most important one. Unfortunately, "palliation" is so subjective and elusive a quality that it defies any effort to reduce it to a statistical basis, and few have attempted to do so.

Surprisingly few reports have yet appeared to substantiate the firm clinical impression that resection of solitary, circumscribed, peripheral lesions will yield results superior to those of resection of carcinoma in general. That such lesions are carcinoma in a high proportion of cases has been clearly established, although great difficulty is encountered in arriving at any standard method of defining what a "coin" lesion, or a "silent" cancer of the lung may be.[41-44] As in the differential diagnosis of mediastinal tumors, there are relatively few reliable criteria upon which to rule carcinoma in or out short of exploration. The presence of radiologically demonstrable calcium in a peripheral, rounded lesion is perhaps the only reasonably reliable guide to a benign lesion — either a focal area of tuberculosis or a hamartoma.

It is worth while to consider again the results of the mass survey conducted recently in Boston and reported in this journal.[45] Of 536,012 cases surveyed, the radiologic findings were suggestive of carcinoma in 398, and in 39, primary bronchogenic carcinoma was proved. Of these, 22 patients underwent successful resection, and 5 survived for three years or more. Such figures should not be construed as showing the futility of operation, but they do emphasize the futility of a single survey of all age groups as a method of *cancer* control. This was, of course, recognized in the survey, which was part of a *tuberculosis* control program and did not specifically concern carcinoma. The directors of that survey made the following comment:

> A single survey, although it may provide useful and interesting information, can have no significant effect on the control of lung cancer. To be effective and to detect new, early lesions as they develop, it must be repeated indefinitely at intervals of not more than four or six months and must cover a substantial percentage of the population in the affected age groups.

The question of the association of carcinoma and cigarette smoking continues on its controversial way in medical and lay journals, in editorial pages and advertising mediums. The problem has been the subject of a series of editorials in this journal.[46] It seems fair to point out that there are still *two* sides to the question.[47]

In the past few years there has been a growing interest in "scalene-node biopsy" in the diagnosis of obscure pulmonary conditions.[48] So far as this has called attention to the need for careful physical examination of the patient with suspected carcinoma, it has been an excellent thing. The frequency of metastasis to supraclavicular nodes from cancer of the lung is well known, and the careful removal of such nodes, especially when palpable, to make a diagnosis has long been accepted. It is difficult to know how often scalene-node biopsy, in the absence of palpable nodes, will provide useful information. The evidence suggests that it is extremely useful in establishing the diagnosis in Boeck's sarcoid. So far as cancer is concerned, when nodes are palpable, the percentage of positive explorations should be high — when nodes are not felt, various estimates of up to 40 per cent have been made.[49-51]

The concept of an anatomic entity—"a scalene node"—is useful so far as it requires the surgeon to systematize his technical approach to a deep cervical node. Whether such an approach should be extended to include exploration of the upper mediastinum through a small cervical incision is a matter of debate,[52] particularly in view of the increasing use of what may be called "radical" pneumonectomy in the sense of "radical" mastectomy. The nodes of the upper mediastinum, particularly on the right, are resectable in continuity with the lung. How far such an extension of pneumonectomy will benefit a group of patients, both as a matter of long-term survival and for control of symptoms, is a matter of conjecture. No conclusive statistics are yet available, nor is the value of combined surgical and radiation therapy in patients with positive mediastinal nodes established.

As might have been anticipated, angiocardiography has proved useful in predicting the unresectability of bronchial carcinoma. Slesser et al.[53] have reported a series of 31 patients studied in this manner. In 11 of these distortion of the superior vena cava or the pulmonary artery was found, suggesting invasion. In all 11, resection proved to be impossible, although clinically and bronchoscopically the lesions were judged to be operable.

Obstruction of the superior vena cava is most commonly associated with inoperable carcinoma of the lung. There are a few cases, however, in which it is the result of benign disease. Under these circumstances it rarely produces symptoms severe enough to warrant surgical interference. In the occasional case in which this is true, however, surgical reconstruction of the superior vena cava is possible through the use of venous or preserved blood-vessel grafts.[54]

Alveolar-cell carcinoma of the lung continues to intrigue clinician and pathologist alike. This is a rare tumor, but one that has been reported with increasing frequency. The process is usually a diffuse one, and multicentric origin of the tumor has been claimed and denied. The characteristic profuse, glairy secretion has been shown to be a late manifes-

tation of the disease. Cytologic examination of the sputum, however, has proved very rewarding even in the early cases, in which surgical excision may be quite successful. The subject has been comprehensively reviewed by Storey, Knudtson and Lawrence.[55]

Clagett has called attention to an interesting syndrome of pulmonary osteoarthropathy and arthritis associated with localized fibrous mesothelioma of the pleura. He and his associates[56] present 24 such patients from the records of the Mayo Clinic. In these cases, the systemic symptoms of joint pain, chills and fever were otherwise unexplained but were relieved by removal of the pleural tumor, which was classified as malignant on the basis of its histology and tendency to recur, though definite evidence of metastasis was lacking. The syndrome of pulmonary osteoarthropathy in conjunction with fibrous tumors of the pleura has also been reported by Benoit and Ackermann,[57] in St. Louis, and Thomas and Drew,[58] of London.

Paulson and Shaw[59] have made a noteworthy contribution in their presentation of 21 cases in which bronchial anastomosis or bronchoplastic procedures patterned after the Gebauer technic were used in the interests of preserving functional lung tissue. It is interesting that 12 of the 16 patients had primary bronchogenic carcinoma. In 4 of these lobectomy was done because, in the authors' opinion, the patient would not have tolerated pneumonectomy and the preservation of functioning lung tissue, even if it meant reimplantation of a bronchus, was strongly indicated. In 6 cases the authors deliberately chose local excision and reanastomosis for small, centrally located tumors. In 2, reimplantation of a divided bronchus was necessary to widen the limits of operability for a tumor extending into the lower trachea. One patient died twelve days after an end-to-end anastomosis of the left main bronchus to the trachea that followed resection of the right lung. Three patients died of their carcinoma within a year of operation. The remaining 8, including all those in whom the operation was chosen deliberately for small central lesions, were alive and well for varying periods up to twenty-six months after operation. The authors rightly call attention to the amazing healing powers of the bronchus if handled in such a manner as to permit healing by first intention.

The use of conservative operations has been well illustrated in the experience with bronchial adenomas that Soutter et al.[60,61] have presented. The totally different behavior of such tumors in comparison with that of bronchogenic carcinoma is well shown, and if further evidence is needed on the point, the limitations and dangers of bronchoscopic treatment of these tumors are presented.

Tumors of the trachea continue to pose difficult problems of management although sporadic cases of resection and tracheal replacement appear.[62,63] Minor[64] and Kleitsch[65] both report cases in which transternal excisions of tracheal tumors followed by anterior mediastinal tracheotomies have been successfully carried out. Unfortunately, malignant tumors of the trachea unless small are usually unresectable by virtue of their proximity to unexpendable structures.

Tuberculosis

The subject of tuberculosis quite properly merits a progress report of its own. This has been written by King,[66] who notes that resection therapy for tuberculosis is now well established in this country, although thoracoplasty yielded good results in the past[67,68] and bronchial fistulas still occur after resection.[69] It is quite clear, however, that the results of surgical excision as a selective method of treatment have been good, including the highly selective procedure of segmental resection when the interpretation of the pathologic state of the tuberculosis is correct.[70,71] Not only are the early results of resection good but also the late results are standing up well.[72] The same thing, of course, can be said of thoracoplasty, and a differential analysis of relative merit on the basis of published statistics is exceedingly difficult.[73,74]

One gains the impression that in European centers thoracoplasty enjoys greater popularity than in this country.[75] The reasons for this are not entirely clear except that it is difficult to abandon a procedure that has a low mortality and excellent results. Both Brock[76] and Björk[77] have made valuable suggestions in the technic of thoracoplasty to minimize the number of ribs resected and yet to provide early, fixed and adequate collapse. To accomplish this they describe an osteoplastic procedure whereby a hinged, bony flap is fashioned and swung down over the collapsing upper portions of the lung.

The therapy of tuberculosis, surgical or otherwise, is frequently described in terms that have great significance to the initiated but are not always clear to the outsider. One of the latest of such terms is "target point" as applied to chemotherapy of the disease. "Target point" denotes the stage at which sputum and gastric specimens become negative by culture and, by x-ray examination, there is closure of any cavity and the lesion appears to be stable. If, under antibiotics and chemotherapy, the patient fails to reach the target point in a reasonable length of time after the institution of therapy — usually four to six months — surgical intervention is to be strongly considered, for in this group relapses are likely to occur.[78] If, on the other hand, residual nodular lesions are present after the target point has been reached, resection is considered to be safe.[79]

The problem of resection of residual caseous lesions in pulmonary tuberculosis is far from settled; in fact O'Brien and his associates,[80] with more than a little justification, describe the present situation as confusing and chaotic. As they point out, scars or "nubbins" are present in many thousands of people

throughout the country, and most of them are, and have been for years, living normal lives. The argument for widespread resection is that the patient's future would be less hazardous if all lesions, including "nubbins," were removed. It is also true that a patient is better off with no surgery at all if he does not need it. A serious, painful mental and physical experience should not be taken lightly. On the other hand the problem of recognizing an inspissated cavity among residual lesions is important, for viable organisms of indeterminate virulence can be recovered from such lesions in a high proportion of cases.[81]

The continuing value of streptomycin in the surgical management of tuberculosis is self-evident. It is of some historical interest that it is now ten years since the first patient, a twenty-one-year-old girl with progressive, far-advanced pulmonary tuberculosis, was treated with streptomycin. The patient is still alive and well and leading a very active life.[82]

Mycotic Infections

The pulmonary lesions of coccidioidomycosis, histoplasmosis and blastomycosis — to name the three most common mycotic infections of the lung — are so often indistinguishable from tuberculosis or neoplasm that they frequently come to the attention of the thoracic surgeon.

Coccidioidomycosis is perhaps the best known of the three, especially in the Southwest, where it is endemic. It is quite clear that its nodular peripheral lesion may progress to cavitation and occasionally to dissemination. Cavities, also, may become secondarily infected or break through into the pleural space. As Greer, Forsee and Mahon[83] and Guilfoil[84] have shown, an aggressive surgical approach to cavitary or localized disease has been worth while. No specific antibiotic has been found that is particularly effective; yet extirpative surgery for this disease has been reasonably safe. Antigenic material for skin testing, coccidioidin, is commercially available, to be used in a manner similar to tuberculin, and having comparable significance.

Histoplasma capsulatum is enjoying a clinical career similar to that of *Coccidioides immitis*. It is known to give rise to a generalized and sometimes fatal disease; it is suspected of being responsible for scattered pulmonary calcifications (especially in the absence of a positive tuberculin skin test), and it may also be found as a focal lesion similar to the so-called "tuberculoma." As Forsee et al.[85] have pointed out, when focal pulmonary lesions of histoplasmosis are recognized, there is a marked decline in the incidence of pulmonary lesions classified as tuberculomas in which the tubercle bacillus cannot be recognized. Local excision of such focal lesions has been shown to be safe.

Pulmonary manifestations of blastomycosis are less common than the preceding two, but more serious when they occur. The subject has been well reviewed by Acree, DeCamp and Ochsner.[86] The fungus, *Blastomyces dermatididis*, causes cutaneous and visceral lesions with equal frequency, it is a systemic disease and may be treated effectively with stilbamidine, which is a relatively toxic agent, or some of its less toxic derivatives. The pulmonary lesions of blastomycosis often result from endobronchial lesions similar to the cutaneous manifestations of the disease. Experience to date[87-89] indicates that pulmonary resection in unsuspected cases of pulmonary blastomycosis is hazardous and should be promptly followed by diamidine therapy.

Esophagus

Tumors

A recent report by Sweet[90] clearly illustrates the effectiveness of surgery in the treatment of cancer of the esophagus. He points out that if, as in cancer of other viscera, the emphasis in this disease is placed on the hope of cure, the number of patients operated on will be small. If the intent is to provide relief from the discomforts of a disease and possible cure in the favorable case, operation will be offered to a greater number of patients. He has adopted the latter attitude and reports the late results in 450 patients in whom resection was carried out in the years 1939-1952.

Of these, 17 had carcinoma in the cervical zone, and in 10 resection was possible according to the Wookey technic. There were no operative deaths; there was excellent relief of dysphagia, but 7 patients ultimately died of the disease. Two were surviving at eighteen months, and 1 had only recently been operated on. The impression is fairly widespread that cancer of the cervical esophagus can equally well be treated by radiation. Statistical confirmation of this impression is difficult to find. However, Jørgsholm,[91] in Sweden, has reported 67 patients with carcinoma of the extrathoracic portion of the esophagus treated with generous dosages of x-rays (3200 — 10,200 r). Of the 67, 18 were free of symptoms at one year, 11 at two years, 10 at three years, and 8 at four and five years.

Sweet admits some discouragement with cancer of the superior mediastinal segment of the esophagus. Of 9 such patients explored, he was able to resect the tumor in 6, with an operative mortality of 50 per cent. No patient survived longer than twenty-six months. As he points out, the technical difficulties of resection for cancer at this level are the greatest of any location in the esophagus, and the prospect of adequate removal of involved regional lymph nodes is exceedingly unfavorable. In an attempt to extend the field of operation and facilitate exposure Waddell[92] has recently proposed an anterior, sternum-splitting incision for carcinoma of the lower cervical and superior mediastinal segments. He has carried this out in 4 patients and found that an anterior approach provided excellent access to this difficult zone.

Carcinoma of the midthoracic segment of the esophagus — the portion adjacent to the arch of the aorta — is much more common than carcinoma of the cervical or superior mediastinal segments. It is not a zone that promises a high percentage of long-term survivors — in Sweet's series, 4 per cent of those in whom resection is possible. In other terms than actual survival, however, the operation has been judged worth while. Furthermore, Sweet notes that if "palliative" operations (in the sense that known tumor was left behind at operation) were excluded, 14 per cent of patients surviving operation lived for more than five years. Adams et al.[93] have professed such great discouragement with resection of tumors at this level that they propose combining postoperative irradiation with all resections. The results of such combined therapy are not yet on record. Sporadic reports of by-passing technics using plastic prostheses have appeared, and "palliation" has been reported.[94-96] The subject is hardly a settled one, but for the present, the optimistic agressive approach seems to be the sounder one.

Cancers of the lower end of the esophagus and cardia of the stomach are reasonably favorable tumors. To return to Sweet's series, there were 242 patients with tumors at this level. Resection was possible in 167; 147 survived operation, and of these 17 per cent survived for five or more years. If "palliative" resections in this group were excluded, 34 per cent survived for five or more years. Garlock and Klein[97] report similar figures.

The over-all picture regarding radiation alone for cancer of the esophagus is not bright, although it is remarkable how frequently relief of obstructive symptoms can be effected. Relatively few long-term survivals have been reported — usually measured in terms of a few per cent.[98-100]

In the last few years a number of reports have appeared dealing with the subject of benign tumors of the esophagus, either cysts or, more commonly, smooth-muscle tumors of the esophageal wall.[101,102] Such tumors may or may not be symptomatic, depending usually on their size. Unless they are bulky, simple enucleation is universally agreed to be adequate. Sarcoma of the esophagus is rare, although Sweet, Soutter and Tejada[103] report 2 malignant tumors in a series of 22 muscle-wall tumors. A bibliography of benign tumors and cysts of the esophagus is included in the paper by Totten et al.[104] published in 1953.

Benign Obstruction of the Lower End of the Esophagus

There is an interesting newcomer to the group of diseases affecting the lower end of the esophagus — namely, dysphagia produced by a contractile ring or diaphragm-like, localized narrowing in the lower esophagus, described independently by Ingelfinger and Kramer[105] and Schatzki and Gary.[106] Both groups of authors agree that the condition can be differentiated from achalasia or cardiospasm, fibrosis, esophagitis and hiatal hernia. The condition or syndrome consists of dysphagia and a constant ring-filling defect about 1 cm. above the level of the diaphragm. Esophagoscopic examination of the area has generally been disappointing; surgical relief is rarely necessary, and autopsy material fortuitous and not characteristic. It is clear that further observations will be needed before the syndrome can be defined or accepted.

Not a great deal of definitive information has been added to the subject of benign esophagitis with or without hiatus hernia, except that as the smoke clears, it is apparent that the subject is inextricably bound in with the problems of peptic ulcer. The subject is complex enough to merit a progress report of its own.

Miscellaneous Conditions

Burford, Webb and Ackerman[107] have reported on caustic burns of the esophagus and their surgical management. Their experimental studies of lye burns of the esophagus in dogs have shown the importance of invasive infection early in the evolution of the disease and the relatively slow process of epithelization. Both factors suggest that early, vigorous dilatation is to be condemned. In a series of 17 clinical cases, they carried out resection with esophagogastrostomy in 13 and end-to-end suture for narrow stricture in 4. There were no operative deaths, no significant complications and excellent functional results. On the basis of their experience, they conclude that early operation is advisable unless dilatations go very easily from the start.

For a number of years, tracheoesophageal fistula in the newborn infant has presented real difficulties if primary reconstitution of continuity is not possible. A number of delayed methods of reconstruction have been proposed.[108-112] The most recent proposal, by Dale and Sherman, of Rochester,[113] is the use of the ascending colon transplanted into the neck by way of an anterior mediastinal tunnel. Of great advantage is the fact that the operation can be carried out early in infancy and yet avoids a disastrous "all-or-none" policy in the newborn infant.

Discussion

By way of conclusion, I should like to call attention to a number of excellent textbooks on the subject of thoracic surgery that have appeared in the last few years. Of special note, perhaps, are those of Lindskog and Liebow,[114] D'Abreu,[115] Gross[116] and Sweet.[117]

References

1. Linton, R. R., and Hardy, I. B., Jr. Treatment of thoracic aortic aneurysms by "pack" method of intrasaccular wiring. *New Eng. J. Med.* **246**:847-855, 1952.
2. Bahnson, H. T. Definitive treatment of saccular aneurysms of aorta with excision of sac and aortic suture. *Surg., Gynec. & Obst.* **96**:383-402, 1953.
3. *Idem.* Considerations in excision of aortic aneurysms. *Ann. Surg.* **138**:377-386, 1953.
4. Stranahan, A., Alley, R. D., Sewell, W. H., and Kausel, H. W. Aortic arch resection and grafting for aneurysm employing external shunt. *J. Thoracic Surg.* **29**:54-65, 1955.

5. Mahorner, H., and Spencer, R. Shunt grafts: method of replacing segments of aorta and large vessels without interrupting circulation. *Ann. Surg.* **139**:439-446, 1954.
6. Hardin, C. A., Reismann, K. R., and Dimond, E. G. Use of hypothermia in resection and homologous graft replacement of thoracic aorta. *Ann. Surg.* **140**:720-725, 1954.
7. Cooley, D. A., and DeBakey, M. E. Resection of thoracic aorta with replacement by homograft for aneurysms and constrictive lesions. *J. Thoracic Surg.* **29**:66-104, 1955.
8. Hollingsworth, R. K., Johnston, W. W., and McCooey, J. F. Traumatic saccular aneurysm of thoracic aorta. *J. Thoracic Surg.* **24**:325-345, 1952.
9. Boyden, E. A. *Segmental Anatomy of the Lungs: A study of the segmental bronchi and related pulmonary vessels.* 276 pp. New York: McGraw-Hill, 1955.
10. Rouvière, H. *Anatomy of the Human Lymphatic System: A compendium tr. from the original Anatomie des lymphatiques de l'homme, and rearranged for the use of students and practitioners, by M. J. Tobias.* 318 pp. Ann Arbor: Edwards, 1938.
11. Hahn, P. F., and Carothers, E. L. Lymphatic drainage following intrabronchial instillation of silver-coated radioactive gold colloids in therapeutic quantities. *J. Thoracic Surg.* **25**:265-279, 1953.
12. Meneely, G. R., Auerbach, S. H., Woodcock, C. C., Kory, R. C., and Hahn, P. F. Transbronchial instillation of radioactive gold colloid in lung of dog: distribution studies, survival and pathology. *Am. J. M. Sc.* **225**:172-177, 1953.
13. Weinberg, J. A. Identification of regional lymph nodes in treatment of bronchogenic carcinoma. *J. Thoracic Surg.* **22**:517-526, 1951.
14. Churchill, E. D. Architectural basis of pulmonary ventilation. *Ann. Surg.* **137**:1-11, 1953.
15. Comroe, J. H., et al. *The Lung: Clinical physiology and pulmonary function tests. (Based on the 1954 Beaumont Lecture.)* 219 pp. Chicago: Year Book Publishers, 1955.
16. Woodruff, W., Merkel, C. G., and Wright, G. W. Decisions in thoracic surgery as influenced by knowledge of pulmonary physiology. *J. Thoracic Surg.* **26**:156-183, 1953.
17. Gaensler, E. A., et al. Role of pulmonary insufficiency in mortality and invalidism following surgery for pulmonary tuberculosis. *J. Thoracic Surg.* **28**:163-187, 1955.
18. Björk, V. O. Cardiopulmonary function tests. *J. Thoracic Surg.* **26**:67-85, 1953.
19. Adams, W. E., Perkins, J. F., Jr., Flores, A., Chao, P., and Castellanos, N. Significance of pulmonary hypertension as cause of death following pulmonary resection. *J. Thoracic Surg.* **26**: 407-418, 1953.
20. Carlens, E., Hanson, H. E., and Nordenström, B. Temporary unilateral occlusion of pulmonary artery: new method of determining separate lung function and radiologic examinations. *J. Thoracic Surg.* **22**:527-536, 1951.
21. Sloan, H., Morris, J. D., Figley, M., and Lee, R. Temporary unilateral occlusion of pulmonary artery in preoperative evaluation of thoracic patients: preliminary report. *J. Thoracic Surg.* **30**:591-597, 1955.
22. Nemir, P., Jr., Stone, H. H., Mackrell, T. N., and Hawthorne, H. R. Controlled unilateral bronchovascular occlusion as method for studying pulmonary function. *Surgery* **34**:401-411, 1953.
23. Kaunitz, V. E., and Andersen, M. Experimental study of effect of parasympathetic denervation of lung on pulmonary artery pressure. *J. Thoracic Surg.* **27**:55-63, 1953.
24. Abbott, O. A., VanFleit, W. E., Roberto, A. E., and Salomone, P. P. Studies on function of human vagus nerve in various types of intrathoracic disease. *J. Thoracic Surg.* **30**:564-590, 1955.
25. Sloan, H. Lobar obstructive emphysema in infancy treated by lobectomy. *J. Thoracic Surg.* **26**:1-20, 1953.
26. Henry, W. Localized pulmonary hypertrophic emphysema. *J. Thoracic Surg.* **27**:197-203, 1954.
27. Editorial. Bronchiectasis. *Lancet* **2**:489, 1955.
28. Perry, K. M. A., and King, D. S. Bronchiectasis: study of prognosis based on follow-up of 400 patients. *Am. Rev. Tuberc.* **41**:531-548, 1940.
29. Paterson, J. F. Disappointing results of pulmonary resection for bronchiectasis. *Canad. M. A. J.* **66**:433, 1952.
30. Overholt, R. H., Walker, J. H., and Etsten, B. Pulmonary function after multiple segmental resection for bronchiectasis. *J. Thoracic Surg.* **25**:40-54, 1953.
31. Lindskog, G. E., and Alley, R. D. Bilateral bronchiectasis: analysis of 43 consecutive cases. *Arch. Surg.* **60**:465-472, 1950.
32. Kergin, F. G. Surgical treatment of bilateral bronchiectasis. *J. Thoracic Surg.* **19**:257-269, 1950.
33. Ginsberg, R. L., Cooley, J. C., Olsen, A. M., and Kirklin, J. W. Analysis of unfavorable results in surgical treatment of bronchiectasis. *J. Thoracic Surg.* **30**:331-334, 1955.
34. Wisoff, C. P., and Felson, B. Bronchography with oily Dionosil. *J. Thoracic Surg.* **29**:435-446, 1955.
35. Bernstein, A. Selective segmental bronchography with water-soluble contrast media. *Brit. J. Radiol.* **27**:97-106, 1954.
36. Peck, M. E., Neerken, A. J., and Salzman, E. Clinical experience with water-soluble bronchography compounds. *J. Thoracic Surg.* **25**:234-245, 1953.
37. Waddell, W. R., Sniffen, R. C., and Whytehead, L. L. Etiology of chronic interstitial pneumonitis associated with lipid deposition: experimental study. *J. Thoracic Surg.* **28**:134-144, 1954.
38. Gibbon, J. H., Jr., Stokes, T. L., and McKeown, J. J., Jr. Surgical treatment of carcinoma of lung. *Am. J. Surg.* **89**:484-493, 1955.
39. Gibbon, J. H., Jr., Allbritten, F. F., Jr., Templeton, J. Y., III, and Nealon, T. F., Jr. Cancer of lung: analysis of 532 consecutive cases. *Ann. Surg.* **138**:489-501, 1953.
40. Boyd, D. P., Smedal, M. I., Kirtland, H. B., Jr., Kelley, G. E., and Trump, J. G. Carcinoma of lung: report of 403 cases. *J. Thoracic Surg.* **28**:392-411, 1954.
41. Hood, R. T., Jr., Good, C. A., Clagett, O. T., and McDonald, J. R. Solitary circumscribed lesions of lung: study of 156 cases in which resection was performed. *J.A.M.A.* **152**:1185-1191, 1953.
42. Wilkins, E. W., Jr. Asymptomatic isolated pulmonary nodule. *New Eng. J. Med.* **252**:515-520, 1955.
43. Tuttle, W. M., Barrett, R. J., and Hertzler, J. H. Importance of surgery in management of pulmonary coin lesion. *Am. J. Surg.* **89**:422-424, 1955.
44. Overholt, R. H., Bougas, J. A., and Woods, F. M. Surgical treatment of lung cancer found on x-ray survey. *New Eng. J. Med.* **252**:429-432, 1955.
45. McNulty, J. M. Clinical follow-up study of 398 patients suspected of having lung cancer discovered in Boston chest x-ray survey. *New Eng. J. Med.* **250**:14-17, 1954.
46. Editorial. Scientific perspective. *New Eng. J. Med.* **250**:923, 1954.
47. Engel, L. Do we have to give up smoking? *Harpers* **209**:25-30, 1954.
48. Daniels, A. C. Method of biopsy useful in diagnosing certain intrathoracic diseases. *Dis. of Chest* **16**:360-366, 1949.
49. Seghers, K. K. M. F., Orie, N. G. M., Hadders, H. N., and Nunderhout, J. M. Daniels' biopsy in diagnosis and treatment of pathologic processes in lungs and mediastinum. *Arch. chir. Neerl.* **6**:57-64, 1954.
50. Cuykendall, J. H. Use of prescalene lymph node biopsy in absence of palpable supraclavicular nodes: report of 41 cases. *J.A.M.A.* **155**:741, 1954.
51. Piper, C. A. Scalene node biopsy in diagnosis of diseases of chest. *Am. Pract.* **5**:182, 1954.
52. Harken, D. E., Black, H., Clauss, R., and Farrand, R. E. Simple cervicomediastinal exploration for tissue diagnosis of intrathoracic disease: with comments of recognition of inoperable carcinoma of lung. *New Eng. J. Med.* **251**:1041-1044, 1954.
53. Slesser, B. V., Britt, R. G., and Freer, J. L. Assessing inoperability of bronchial carcinoma by angiocardiography. *Thorax* **9**: 91-99, 1954.
54. Scannell, J. G., and Shaw, R. S. Surgical reconstruction of superior vena cava. *J. Thoracic Surg.* **28**:163-174, 1954.
55. Storey, C. F., Knudtson, K. P., and Lawrence, B. J. Bronchiolar (alveolar cell) carcinoma of lung. *J. Thoracic Surg.* **26**:331-406, 1953.
56. Clagett, O. T., McDonald, J. R., and Schmidt, H. W. Localized fibrous mesothelioma of pleura. *J. Thoracic Surg.* **24**:213-230, 1952.
57. Benoit, H. W., Jr., and Ackermann, L. V. Solitary pleural mesotheliomas. *J. Thoracic Surg.* **25**:346-357, 1953.
58. Thomas, C. P., and Drew, C. E. Fibroma of visceral pleura. *Thorax* **8**:180-188, 1953.
59. Paulson, D. L., and Shaw, R. R. Bronchial anastomosis and bronchoplastic procedures in interest of preservation of lung tissue. *J. Thoracic Surg.* **29**:238-259, 1955.
60. Soutter, L. 31-year hospital experience with bronchoscopic approach to bronchial adenoma. *Ann. Otol., Rhin. & Laryng.* **63**: 509-519, 1954.
61. Soutter, L., Sniffen, R. C., and Robbins, L. L. Clinical survey of adenomas of trachea and bronchus in general hospital. *J. Thoracic Surg.* **28**:412-430, 1954.
62. Abbott, O. A., VanFleit, W. E., and Roberto, A. E. Experiences with extending indications for use of tracheal and bronchial grafts. *J. Thoracic Surg.* **29**:217-237 and 252, 1955.
63. Cotton, B. H., and Penido, J. R. F. Resection of trachea for carcinoma: report of 2 cases. *J. Thoracic Surg.* **24**:231-245, 1952.
64. Minor, T. Trans-sternal tracheal excision for carcinoma: report of case. *J. Thoracic Surg.* **24**:88-92, 1952.
65. Kleitsch, W. P. Anterior mediastinal tracheotomy. *J. Thoracic Surg.* **24**:38-42, 1952.
66. King, D. S. Tuberculosis. *New Eng. J. Med.* **252**:94-100 and 135-141, 1955.
67. Aufses, A. H., and Harte, M. S. Results of thoracoplasty for pulmonary tuberculosis eleven to sixteen years after operation: complete follow-up report. *J. Thoracic Surg.* **25**:329-335, 1953.
68. Douglass, R., and Bosworth, E. B. After-history of pulmonary tuberculosis. II. Thoracoplasty: ten-year follow-up. *Am. Rev. Tuberc.* **69**:930-939, 1954.
69. Murphy, J. D., Becker, B. B., and Swindell, H. V. Complications and results of treatment of bronchopleural fistula following resection for tuberculosis. *J. Thoracic Surg.* **24**:578-586, 1952.
70. Chamberlain, J. M., Storey, C. F., Klopstock, R., and Daniels, C. F. Segmental resection for pulmonary tuberculosis: 300 cases. *J. Thoracic Surg.* **26**:471-485, 1953.
71. Eerland, E. D., and Seghers, K. K. M. F. Segmental resection in pulmonary tuberculosis. *Dis. of Chest.* **27**:165-178, 1955.
72. Douglass, R., Bosworth, E. B., Judd, J. M., and Chang, K. H. Resection surgery in tuberculosis: complications and after-history. *J. Thoracic Surg.* **29**:136-150, 1955.
73. Hughes, F. A., Lowry, C. C., and Polk, J. W. Thoracoplasty and resection for pulmonary tuberculosis. *J. Thoracic Surg.* **25**: 454-467, 1953.
74. Baffes, T. G., Schlotterbeck, P., and DeCamp, P. T. Comparison of thoracoplasty and resection therapy in pulmonary tuberculosis. *J. Thoracic Surg.* **27**:349-360, 1954.
75. Sellors, T. H., Nuboer, J. F., Berard, M., Maret, G., and Galy, P. Discussion on surgical treatment of pulmonary tuberculosis. *Internat. Abst. Surg.* **98**:232-235, 1954.
76. Brock, R. Osteoplastic thoracoplasty. *Thorax* **10**:1-8, 1955.
77. Björk, V. O. Thoracoplasty: new osteoplastic technique. *J. Thoracic Surg.* **28**:194-211, 1954.
78. Raleigh, J. W., D'Esopo, N. D., Osgood, C. K., and Campbell, A. H. Surgical treatment and nonpulmonary tuberculosis: relapse following chemotherapy for pulmonary tuberculosis. *Tr. Nat. Tuberc. A.* **50**:260-263, 1954.
79. Falk, A., and Tucker, W. B. Surgical treatment and nonpulmonary tuberculosis: resection failures in pulmonary tuberculosis: follow-up study of 310 patients. *Tr. Nat. Tuberc. A.* **50**:254-259, 1954.
80. O'Brien, E. J., Miller, A. C., Chapman, P. T., Koster, K., and O'Rourke, P. V. Present chaos regarding resection of residual caseous lesions in pulmonary tuberculosis. *J. Thoracic Surg.* **26**: 441-446, 1953.
81. Auerbach, O., Hobby, G. L., Small, M. J., Lenert, T. F., and Comer, J. V. Clinicopathologic significance of demonstration of viable tubercle bacilli in resected lesions. *J. Thoracic Surg.* **29**: 109-135, 1955.

82. Pfuetze, K., Pyle, M. M., Hinshaw, H. C., and Feldman, W. H. First clinical trial of streptomycin in human tuberculosis. *Am. Rev. Tuberc.* **71**:752-754, 1955.
83. Greer, S. J., Forsee, J. H., and Mahon, H. W. Surgical management of pulmonary coccidioidomycosis in focalized lesions. *J. Thoracic Surg.* **18**:591-604, 1949.
84. Guilfoil, P. H. Surgical therapy for pulmonary coccidioidomycosis. *Am. Surgeon* **19**:975-980, 1953.
85. Forsee, J. H., Puckett, T. F., and Hagman, F. E. Surgical considerations in focalized pulmonary histoplasmosis. *J. Thoracic Surg.* **26**:131-139, 1953.
86. Acree, P. W., DeCamp, P. T., and Ochsner, A. Pulmonary blastomycosis: critical analysis of medical and surgical therapies, with report of six cases. *J. Thoracic Surg.* **28**:175-193, 1954.
87. Weisel, W., and Landis, F. B. Endobronchial lesions in pulmonary blastomycosis. *J. Thoracic Surg.* **25**:570-581, 1953.
88. Sealy, W. C., Collins, J. P., and Menefee, E. E. Pulmonary blastomycosis: influence of immunologic findings on selection of patients for operation. *J. Thoracic Surg.* **27**:238-243, 1954.
89. Buechner, H. A., Anderson, A. E., Strug, L. H., Seabury, J. H., and Peabody, J. W., Jr. Pulmonary resection in treatment of blastomycosis. *J. Thoracic Surg.* **25**:468-479, 1953.
90. Sweet, R. H. Late results of surgical treatment of carcinoma of esophagus. *J.A.M.A.* **155**:422-425, 1954.
91. Jørgsholm, B. Roentgen therapy in cancer of extrathoracic portion of oesophagus. *Acta radiol.* **38**:61-78, 1952.
92. Waddell, W. R. Personal communication.
93. Adams, H. D., Hare, H. F., Davis, W. L., Trump, J. G., and Granke, R. C. Treatment of carcinoma of esophagus and cardia by resection and postoperative supervoltage roentgen rays. *Ann. Surg.* **138**:631-642, 1953.
94. Berman, E. F. Experimental replacement of portions of esophagus by plastic tube. *Ann. Surg.* **135**:337-343, 1952.
95. Shackelford, R. T., and Sparkuhl, K. Palliative resection of esophagus with use of plastic tube: case report with autopsy findings. *Ann. Surg.* **138**:791-794, 1953.
96. Dumm, J. B., Macmanus, J. E., Anderson, A. A., and McCormick, R. C. Esophageal reconstruction by means of prosthesis: experimental and clinical experience. *J. Thoracic Surg.* **30**:368-376, 1955.
97. Garlock, J. H., and Klein, S. H. Surgical treatment of carcinoma of esophagus and cardia: analysis of 457 cases. *Ann. Surg.* **139**:19-34, 1954.
98. Buschke, F., and Cantril, S. T. Results of supervoltage roentgenotherapy of esophageal carcinoma. *J. Thoracic Surg.* **26**:105-108, 1953.
99. Frimann-Dahl, J. Rotation therapy in cancer of esophagus. *Acta chir. Scandinav.* **103**:421-424, 1952.
100. Scheel, A. Results of radiation treatment of esophageal cancer at Det Norske Radiumhospital. *Acta. chir. Scandinav.* **103**:425-429, 1952.
101. Johnston, J. B., Clagett, O. T., and McDonald, J. R. Smooth-muscle tumours of oesophagus. *Thorax* **8**:251-265, 1953.
102. Boyd, D. P., and Hill, L. D., III. Benign tumors of esophagus. *Ann. Surg.* **139**:312-324, 1954.
103. Sweet, R. H., Soutter, L., and Tejada, C. Muscle wall tumors of esophagus. *J. Thoracic Surg.* **27**:13-35, 1954.
104. Totten, R. S., Stout, A. P., Humphreys, G. H., and Moore, R. L. Benign tumors and cysts of esophagus. *J. Thoracic Surg.* **25**:606-622, 1953.
105. Ingelfinger, F. J., and Kramer, P. Dysphagia produced by contractile ring in lower esophagus. *Gastroenterology* **23**:419-430, 1953.
106. Schatzki, R., and Gary, J. E. Dysphagia due to diaphragm-like localized narrowing in lower esophagus (lower esophageal ring). *Am. J. Roentgenol.* **70**:911-922, 1953.
107. Burford, T. H., Webb, W. R., and Ackerman, L. Caustic burns of esophagus and their surgical management: clinico-experimental correlation. *Ann. Surg.* **138**:453-460, 1953.
108. Leven, N. L., and Varco, R. L. Experiences with operative management of delayed restoration of alimentary continuity in children originally treated by multiple stage procedure for correction of congenital tracheoesophageal defects. *J. Thoracic Surg.* **25**:16-25, 1953.
109. Rienhoff, W. F., Jr. Antethoracal transplantation of stomach in treatment of congenital atresia of thoracic esophagus: preliminary report. *Bull. Johns Hopkins Hosp.* **82**:496-499, 1948.
110. Sweet, R. H. New method of restoring continuity of alimentary canal in cases of congenital atresia of esophagus with tracheo-esophageal fistula not treated by immediate primary anastomosis. *Ann. Surg.* **127**:757-768, 1948.
111. Potts, W. J. Congenital atresia of esophagus: antethoracic placement of stomach followed by intrathoracic transplantation. *J. Thoracic Surg.* **20**:681-688, 1950.
112. Longmire, W. P., Jr. Antethoracic jejunal transplantation for congenital esophageal atresia with hypoplasia of lower esophageal segment. *Surg., Gynec. & Obst.* **93**:310-316, 1951.
113. Dale, W. A., and Sherman, C. D., Jr. Late reconstruction of congenital esophageal atresia by intrathoracic colon transplantation. *J. Thoracic Surg.* **29**:344-356, 1955.
114. Lindskog, G. E., and Liebow, A. A. *Thoracic Surgery and Related Pathology.* 644 pp. New York: Appleton, 1953.
115. D'Abreu, A. L. *A Practice of Thoracic Surgery.* 591 pp. London: Edward Arnold & Co., 1953.
116. Gross, R. E. *The Surgery of Inlancy and Childhood: Its Principles and techniques.* 1000 pp. Philadelphia: Saunders, 1953.
117. Sweet, R. H. *Thoracic Surgery.* Second edition. 381 pp. Philadelphia: Saunders, 1954.

MEDICAL INTELLIGENCE

THE GUILLAIN–BARRE SYNDROME AS A MANIFESTATION OF INFECTIOUS MONONUCLEOSIS

Report of a Case

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NEUROPATHOLOGICAL changes associated with generalized infectious mononucleosis have frequently been described in the medical literature. The case presented below demonstrated a typical picture of the Guillain–Barré syndrome in which the only manifestation of infectious mononucleosis was a markedly positive heterophil-antibody titer with an associated positive titer in the cerebrospinal fluid. To our knowledge this is the first reported case of this type in which no other manifestations of infectious mononucleosis were present.

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CASE REPORT

A 4-year-old girl had apparently been in good health until admission to the hospital on February 23, 1955, when she complained of weakness in her left arm shortly after awaking. The child was sent to the Cincinnati Children's Hospital for investigation. Examination at that time revealed a well developed and well nourished child with head drop and generalized weakness of almost all muscle groups. Spinal tap showed a normal spinal fluid with a protein of 30 mg. per 100 ml. She was admitted to the hospital for observation, and on the following day demonstrated an absence of all deep tendon reflexes and progressive weakness. The white-cell count was 12,400, with 93 per cent neutrophils and 7 per cent lymphocytes. No abnormal cells were seen. X-ray examination of the skull was negative. On February 25 she had two convulsions. There was definite diaphragmatic weakness and a marked tachycardia. She was seen at this point by a neurologist, who noted areflexia and considerable generalized weakness of all extremities, as well as nuchal rigidity. On the next day dysphagia and dysphonia developed, and the temperature rose to 102°F. She had 2 short convulsive episodes, and respiratory distress appeared to be developing. At this point she was transferred to the Contagious Division of the Cincinnati General Hospital with the probable diagnosis of bulbospinal poliomyelitis.

Physical examination revealed an acutely and severely ill child with quadriplegia and pooling of pharyngeal secretions. Respiratory movements were greatly decreased. She responded poorly to pin prick, and a definite hypesthesia from the neck down was noted. A tracheotomy was immediately performed, and she was placed in a tank respirator.

From this point on there was a gradual improvement. On

March 3 the cerebrospinal-fluid protein was 70 mg. per 100 ml. Return of function began with the lower extremities and progressed slowly and steadily upward. A heterophil-antibody titer on March 9 was positive in a dilution of 1:1792. A repeat titer 1 week later was positive in a dilution of 1:448 with the use of the guinea-pig-kidney absorption test. Beef red-cell absorption was negative. An associated positive cerebrospinal-fluid heterophil antibody was obtained at this time. Blood smears during the entire illness failed to reveal the presence of atypical lymphocytes. A methylene blue absorption test for toxoplasmosis performed at Ohio State University was negative. Since improvement continued the tracheotomy tube was removed, and the patient was transferred to the Children's Convalescent Home, where she recovered completely over a period of 3 months, with no residual weakness.

Review of the Literature

The involvement of the central nervous system associated with established cases of infectious mononucleosis has been described for a number of years. Epstein and Dameshek[1] reported a case in 1931 and described a patient admitted to the hospital with fever, chills, headache, generalized lymphadenopathy, abnormal leukocytes in the peripheral blood and pleocytosis in the cerebrospinal fluid. This case was diagnosed as "glandular fever."

Bernstein and Wolf,[2] in 1946, reviewed the central-nervous-system manifestations of infectious mononucleosis and classified the various types[3-8] as follows:

Serous meningitis, as manifested by pleocytosis and elevation of the cerebrospinal-fluid protein. A few cases of this type have been reported, the only abnormality being the elevated protein level.[3]

Encephalitis.[3-5]

Acute polyneuritis.[1,6,7]

Optic neuritis.

In these cases of infectious mononucleosis, most of which were established by positive heterophil-antibody titers, the protean manifestations of the disease were also quite evident. From a review of the literature, it appears that quadriplegia with respiratory-muscle involvement rarely develops to the extent observed in the case reported above. In the majority of cases associated with central-nervous-system involvement other characteristic clinical signs and symptoms of infectious mononucleosis were present: generalized lymphadenopathy, most prominent in the cervical area; frequent sore throat, often with exudate; occasional skin rashes; and generally an abnormal blood picture in either the quantity or the type of lymphocytes. Generally, an elevated heterophil-antibody titer was present.

Course and Prognosis

Characteristically, as with other types of infectious mononucleosis, the outlook in reported cases was good, and recovery was remarkably complete. However, this is not always true. Ricker et al.[7] report 2 deaths from respiratory failure, and Allen and Kellner[8] present autopsy findings on 1 case; in this autopsy there were local collections of "Downey cells" throughout the liver, brain, heart and lungs, along with perivascular cuffing.

Discussion

The case described above was extremely interesting for several reasons. The primary manifestation was the severe central-nervous-system disease, which appeared to be a separate entity in itself. The etiology was completely unknown until the positive heterophil-antibody titer was discovered. None of the usual manifestations of infectious mononucleosis except the markedly positive titer were present. The presence of an elevated cerebrospinal-fluid protein and the absence of cellular elements in the spinal fluid classify this case as the Guillain–Barré type of ascending polyneuritis. We believe, therefore, that in this particular patient the Guillain–Barré syndrome was a manifestation of infectious mononucleosis.

Summary and Conclusions

A case of infectious mononucleosis with transient quadriplegia, respiratory-muscle paralysis and bulbar and cerebral involvement is presented in which the positive heterophil-antibody titer was the only manifestation of the disease besides the neurological findings.

It is suggested that infectious mononucleosis be considered as a possible cause of neurologic disorders of unknown origin, even in the absence of so-called typical signs and symptoms.

References

1. Epstein S. H., and **Dameshek, W.** Involvement of central nervous system in case of glandular fever. *New Eng. J. Med.* **205**:1238-1241, 1931.
2. Bernstein, T., and Wolff, H. G. Involvement of nervous system in infectious mononucleosis. *Ann. Int. Med.* **33**:1120-1138, 1950.
3. Thelander, H. E., and Shaw, E. B. Infectious mononucleosis, with special reference to cerebral complications. *Am. J. Dis. Child.* **61**: 1131-1145, 1941.
4. Landes, R., Reich, J. P., and Perlow, S. Central nervous system manifestations of infectious mononucleosis. *J.A.M.A.* **116**:2482-2484, 1941.
5. Zohman, B. L., and Silverman, E. G. Infectious mononucleosis and encephalomyelitis. *Ann. Int. Med.* **16**:1233-1239, 1942.
6. Hiller, R. I., and Fox, M. J. Infectious neuronitis associated with infectious mononucleosis. *Marquette M. Rev.* **7**:152-154, 1943.
7. Ricker, W., Blumberg, A., Peters, C. H., and Widerman, A. Association of Guillain-Barré syndrome with infectious mononucleosis: with report of 2 fatal cases. *Blood* **2**:217-226, 1947.
8. Allen, F. H., Jr., and Kellner, A. Infectious mononucleosis: autopsy report. *Am. J. Path.* **23**:463-477, 1947.

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42061

PRESENTATION OF CASE

First admission. A sixty-seven-year-old farmer was admitted to the hospital because of abdominal pain.

For two weeks his appetite had been poor. Malaise, with dark urine and light-colored stools, had been noted for a week. Two days before admission, after a heavy meal, severe, colicky, nonradiating pain in the upper abdomen, which progressively worsened, developed. Occasional chills and fever were noted; there were two episodes in which he vomited yellowish-brown material. A stool was described as "white." There had been no melena. He had lost 8 pounds in weight during the two weeks before admission.

Twenty years previously he experienced two days of similar pain. There had been no exposure to solvents or rats. He had not received injections recently. He had drunk alcohol excessively in his youth. There was a past history of dull, intermittent, postprandial, epigastric pain, which was worse in the spring and was relieved by food, especially milk, or induced vomiting.

Physical examination showed a well nourished man complaining of severe pain in the upper abdomen. No jaundice was noted. There was marked epigastric tenderness. The liver edge, which was firm and moderately tender, was felt 1½ fingerbreadths below the right costal margin. One observer felt the tip of the spleen. No abdominal masses were palpable.

The temperature was 100.2°F., the pulse 82, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

Urinalysis was negative. The urinary urobilinogen was 4.6 Ehrlich units. Examination of the blood revealed a hemoglobin of 13 gm. per 100 ml. and a white-cell count of 14,200, with 87 per cent neutrophils. The total protein was 7.4 gm., the albumin 5.1 gm., the globulin 2.3 gm., and the bilirubin 0.6 mg. direct and 1.4 mg. total per 100 ml.; the alkaline phosphatase was 2.6 units, and the amylase 31 Russell units. The bromsulfalein retention was 37 per cent. Cephalin flocculation was ++ in forty-eight hours. Heterophil-antibody agglutination was negative. A stool specimen was light yellow and gave a negative guaiac test. An upper gastrointestinal series demonstrated a small hiatus hernia in the fundus of the stomach. Three Graham tests, the last done on the eighth hospital day, showed poor concentration of the dye.

Except for dull right-upper-quadrant pain and tenderness the abdominal pain subsided on the first hospital day. There was no longer epigastric tenderness. There was marked malaise, however, and increasing jaundice over a period of several days. The liver, which was slightly tender, increased in size, the edge extending to 3½ fingerbreadths below the costal margin, during this time. One examiner felt a nodular liver edge. The temperature ranged between 99.2 and 102°F. A stool on the fifth hospital day was light yellow. The patient was treated with bed rest, and by the seventh hospital day the jaundice had cleared, and the liver edge had regressed to 1 or 2 fingerbreadths below the right costal margin; the urine, stools, temperature and white-cell count were normal, and the serum bilirubin was 0.7 mg. total and the alkaline phosphatase 6 units per 100 ml. He felt better, his appetite returned, and he was discharged on the tenth hospital day with a high-calorie, low-fat diet. The alkaline phosphatase was 5.3 units on the day of discharge.

Second admission (two and a half years later). In the interval he had felt well, gained weight and returned to work. During the four months before admission he had several nocturnal episodes of abdominal pain without fever that were always relieved by a small amount of Demerol. The abdomen was soft during these episodes. Four weeks before entry he was constipated for about five days. Two weeks later he passed loose, somewhat watery, yellowish stools twice daily without cramps, tenesmus or melena. He was otherwise well and continued to work on the farm until three days before admission, when he was awakened at night by severe, steady, aching midabdominal pain, which was not relieved by a bowel movement. The pain persisted and subsequently appeared localized mostly in the middle and lower abdomen. There was associated anorexia. He had forced fluids and occasionally induced vomiting after taking liquids. The vomitus consisted of recently ingested fluids and bile. On the day before entry he experienced substernal and bilateral shoulder pain. The abdomen was soft and nontender, and the temperature was normal. On the morning of the day of admission there was generalized abdominal distention with tenderness, and the temperature was 100.4°F. He had continued to pass a small amount of watery stool daily.

Physical examination revealed a well nourished man who appeared dehydrated. The heart was not enlarged. There was a Grade 1 to Grade 2 apical

systolic murmur, which was transmitted to the aortic area. The rhythm was regular, with occasional premature ventricular beats. There was dullness at both lung bases, with medium dry rales at the left base. The abdomen was distended, tympanitic and tender throughout, with some rebound tenderness in both lower quadrants, especially on the right. Peristalsis

FIGURE 1. *Right Anterior Oblique View of the Stomach and Duodenum, Showing Widening of the Duodenal Loop with Evidence of Extrinsic Pressure on the Inferior Aspect of the Gastric Antrum.*

was minimal. There was no fluid wave. The liver and spleen were not palpable. Rectal examination was negative.

The temperature was 101.4°F., the pulse 100, and the respirations 20. The blood pressure was 130 systolic, 70 diastolic.

Examination of the blood revealed a hemoglobin of 15.5 gm. per 100 ml. and a white-cell count of 13,000. Urinalysis was negative. The nonprotein nitrogen was 25 mg., the alkaline phosphatase 2.1 units, the bilirubin 1.1 mg. and the amylase 8 Russell units per 100 ml.; the serum sodium was 130 milliequiv., the chloride 90 milliequiv., the carbon dioxide 32 milliequiv., and the potassium 3.3 milliequiv. per liter. The prothrombin time was 15 seconds (normal, 13 seconds). The bromsulfalein retention was 21 per cent. Cephalin flocculation was negative in forty-eight hours. An upper gastrointestinal series showed a smooth extrinsic pressure defect on the greater curvature of the stomach in the region of the antrum and questionable widening of the duodenal loop (Fig. 1). Abdominal films demonstrated the ascending and transverse colon distended with air up to the splenic flexure. Barium-enema examination was negative. Films of the chest showed no abnormalities of the heart or lungs. Two stool specimens were normal in color and gave a positive guaiac test; another was negative.

Because of bouts of irregular cardiac rate as high as 160, the patient was digitalized, with a return to a normal rate. By the end of a week the temperature had fallen to normal levels, but it subsequently ranged between normal and 100.4°F. White-cell counts during this period were normal.

On the fifteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. JOSEPH STOKES, III*: In summary, this sixty-seven-year-old farmer had two hospitalizations separated by a symptom-free period of two and a half years. Everything during the first admission indicated a disorder of the liver, and most of the clinical picture, together with the battery of liver-function tests, pointed to hepatocellular disease. However, two features were inconsistent with this diagnosis — the inordinate amount of abdominal pain and the serum amylase of 31 Russell units, which was a mild to moderate elevation. It is apparent from the protocol that the physicians on the service suspected that some type of extrahepatic biliary obstruction might have been present and persisted in getting 3 Graham tests and repeated the alkaline phosphatase, which never rose above 6 units.

The two and a half years between the two admissions is a highly significant period. The patient obviously recovered from the initial illness, gained weight and returned to work. He had, however, several nocturnal episodes of abnormal pain, which were relieved by a small amount of Demerol. A small amount of Demerol is still more than a large dose of aspirin so that those were fairly severe episodes of abnormal pain for which he was apparently seen by a physician. In addition, he had watery, yellowish stools twice daily, suggesting steatorrhea — the stools of pancreatic insufficiency. I wonder whether qualitative or quantitative determinations of the fat were ever done on the stools on either admission.

DR. BENJAMIN CASTLEMAN: None were done.

DR. STOKES: Three days before the second admission a new pain, in the middle and lower abdomen, some substernal and bilateral shoulder pain, indicating subdiaphragmatic irritation, generalized abdominal distention with tenderness — perhaps minimal peritoneal signs — and some degree of ileus developed. The physical examination again showed him to be well nourished — not to have lost a great deal of weight, — and to have mild signs of peritoneal irritation. The serum amylase was normal, and the serum electrolytes suggested the pattern seen with a fair degree of vomiting. The bromsulfalein

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retention was still elevated to 21 per cent. Now, an upper gastrointestinal series showed "a smooth extrinsic pressure defect on the greater curvature of the stomach in the region of the antrum and questionable widening of the duodenal loop." May we look at those films?

DR. C. C. WANG: The x-ray films of the chest and of the barium-enema examination show nothing unusual. Two gastrointestinal series were done in a period of two and a half years. The first series shows a small hiatus hernia; the stomach and duodenum are not unusual. Approximately two and a half years later there is a smooth pressure defect along the greater curvature of the gastric antrum, best seen in the spot films, and some widening of the duodenal loop, which shows an extrinsic pressure defect along its medial aspect (Fig. 1). There is no definite intrinsic involvement of the stomach and duodenum.

DR. STOKES: Is there a peptic ulcer of the duodenal bulb?

DR. WANG: There is no evidence of ulcer. The Graham test shows a poorly functioning gall bladder. There is no evidence of an opaque stone.

DR. STOKES: Is there calcification in the region of the pancreas?

DR. WANG: There is none.

DR. STOKES: What possibilities should be considered in the differential diagnosis? First, infectious hepatitis or homologous serum jaundice might explain the initial illness. As I said before, they fit the clinical picture fairly well except for the inordinate amount of pain, the elevated amylase and the lack of epidemiologic evidence to support infectious hepatitis or homologous serum jaundice. Moreover, a second disease would have to be postulated to explain the second illness.

Could Laënnec's cirrhosis with or without a hepatoma have caused this man's trouble? He gave a history of alcoholism in youth, and the liver was said to be nodular by one observer. However, the initial liver-function tests did not point to chronic liver insufficiency, and certainly he did not have the anatomical picture one would expect with metastatic hepatoma.

Could this represent one of the protean manifestations of peptic ulcer? It is possible that a perforating ulcer in the duodenum initially caused obstruction to the common duct — a rare complication — and that two and a half years later he had a localized, walled-off perforation of the ulcer, which caused the mass seen in the x-ray films. I think we can eliminate this, however, on the basis of the two adequate gastrointestinal series done when he was symptomatic, neither of which gave evidence of peptic ulcer.

One cannot discuss the problem of a colicky right-upper-quadrant pain in an elderly patient without considering biliary-tract disease. However, there were three normal cholecystograms and no reasonable explanation for the mass that developed in the region of the pancreas since it seems inconceivable that the mass represented a single large gallstone.

Carcinoma of the head of the pancreas is by far the most common lesion to produce these x-ray findings. In spite of the low alkaline phosphatase on the initial admission it is possible that the patient had obstruction of the common duct, which was later relieved, and that finally he had an enlarging carcinoma of the pancreas. However, it should be possible to exclude this diagnosis on the basis of the two and a half years during which he was in relatively good health. It is unusual for a carcinoma of the head of the pancreas that had caused common-duct obstruction to cause only some recurrent pain for two and a half years thereafter. A carcinoma of the ampulla of Vater, perhaps, is the exception, but in the patient under discussion the clinical picture was not that of ampullary carcinoma.

Finally, I should like to consider cystic lesions of the pancreas. A variety of pancreatic cysts, such as congenital cysts and cystadenomas, can occur, and in one series of cases of carcinoma of the pancreas, 5 per cent were cystic. There are rare cystic tumors of the pancreas such as dermoids and hemangiomas. Last week Dr. Donald Augustine spoke at medical grand rounds about the prevalence of echinococcus disease fairly close to New England. One could construct a picture of hydatid cyst not only of the liver but also of the pancreas, in which the cysts occur fairly regularly. Rupture of a cyst, with peritonitis, could explain the pain of the second illness. However, I assume that this man was a Yankee farmer and not a Syrian sheepherder and that he had always done his farming in New England.

The most common cystic lesion of the pancreas, the so-called pseudocyst, is not a true cyst at all. To supplement my limited personal experience with these lesions I call attention to a series of 44 cases summarizing the experience at the Mayo Clinic from 1935 through 1947.[1] These lesions can occur anywhere in the pancreas. They are usually of grapefruit size, or perhaps a little larger, and can become so large as to fill the entire upper abdomen. The diagnostic triad is a past history of pancreatitis, the characteristic pain and a palpable abdominal mass. Of the Mayo Clinic's 44 patients, 32 had a mass palpable at the time of operation. The fluid in the cyst is often bloody and occasionally may be purulent, but in 6 out of 7 of their cases the fluid was sterile on culture at the time of operation.

Therefore, returning to this case, I believe that the following is the most likely train of events. On the basis of the past history of abdominal pain the patient had had at least one bout of severe pancreatitis and perhaps had others, and the history of alcoholism and possible cholelithiasis fit in with the history of pancreatitis. During the two and a half years between the first and second admissions a fairly sizable pseudocyst of the pancreas developed in the

area shown on the x-ray films; then the cyst developed either a small leak, which is unusual, or a massive rupture, which is quite rare even in the large cysts, or pancreatitis or some other condition produced the peritoneal signs that he had at the time of the second admission. In addition, because of the initial illness, he probably had some intrinsic liver disease — either a mild degree of Laënnec's cirrhosis or biliary cirrhosis as a result of recurrent cholangitis. I assume that the operation began as a laparotomy to explore the mass, and I hope that a biopsy of the liver was taken.

DR. CASTLEMAN: Dr. Taylor, have you a comment?

DR. GRANTLEY W. TAYLOR: As I read the protocol, I thought that the presumptive diagnoses would be about what Dr. Stokes has summed up. The patient certainly should have been explored. I think that he was lucky to get away the first time without having some surgeon operate on him.

DR. CASTLEMAN: He was on the Medical Service!

DR. WALTER BAUER: I think that Dr. Stokes's diagnosis is correct.

DR. JACOB LERMAN: Is there any evidence of gall-bladder disease in the x-ray films?

DR. WANG: The gall bladder is poorly functioning.

DR. LERMAN: Are any stones visible?

DR. WANG: No.

DR. BAUER: We did have a patient with a cystadenoma of the pancreas who had a story not unlike this.

DR. STOKES: If I could have a second choice, I should choose cystadenoma of the pancreas.

DR. CASTLEMAN: Papillary cystadenomas usually grow slowly and are present for a long time, so that it should have been seen on the first x-ray film.

DR. BAUER: That is a good point.

CLINICAL DIAGNOSIS

Disease in head of pancreas.

DR. JOSEPH STOKES, III'S, DIAGNOSES

Pseudocyst of pancreas.
Pancreatitis, recurrent, acute.
Cirrhosis, Laënnec's or biliary.

ANATOMICAL DIAGNOSIS

Pseudocyst of pancreas, with pancreatic necrosis.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Apparently, the case was not as clear cut as Dr. Stokes has made it appear, because the x-ray film of the gastrointestinal series seems to have been done only a few hours before the patient was operated on. Dr. Quinby, you saw the operation; will you tell us about it?

DR. WILLIAM C. QUINBY, JR.: I wish we had had Dr. Stokes around when this patient entered the Emergency Ward with a fever, a picture of ileus and a large, dilated colon. We thought initially that there was obstruction of the colon, possibly as far down as the sigmoid, and abdominal distention. The abdominal distention responded slowly to the Miller–Abbott tube seen in the films; however, it did not respond completely. The patient began to pass the intestinal contents, but he never became well or really happy. We could feel no abdominal mass. On the basis of the x-ray study we thought that there must be something abnormal in the head of the pancreas; I am not sure what preoperative diagnosis Dr. Robert C. Coe gave. At operation, this was a large inflammatory mass that separated the antrum of the stomach and the transverse colon and presented between the two anteriorly.

A number of times in this hospital, the surgeons have found in the pancreas necrosis that presents the appearance of gray cottage cheese and looks like an abscess full of thick colon-bacillus pus. In this particular case the abscess arose from the midportion and the head of the pancreas and extended down along the superior mesenteric artery, which could be felt pulsating in the base of it. The abscess was merely drained. I believe that the patient's course has progressed well. Culture showed colon bacillus.

DR. CASTLEMAN: We did not receive even a biopsy of the wall of a cyst. We did receive some of the contents of the cyst, but could not make a diagnosis on it. According to the surgeon there was no question that this was a pancreatic cyst. After the operation the drainage from the cyst contained 400 Russell units of amylase so that I gather that that proves it was a pseudocyst, does it not, Dr. Bauer?

DR. BAUER: I have never heard of such a thing.

DR. CASTLEMAN: The patient has left the hospital and has reported several times since to the clinic. The last note, made a few weeks ago, stated that he had gained 14 pounds and felt well, that the wound was solid, that the sinus was closed and that there was no tenderness or redness.

DR. QUINBY: There is a question of semantics, which Dr. Coe and I have argued many times. An uninfected pancreatic pseudocyst and a pancreatic necrosis or abscess without cyst wall are separate clinical entities to me. Two or three weeks before this, the service had a patient with repetitive episodes of pancreatitis, who had had numerous hospital admissions all over the East. He had a mass laterally in the abdomen and at operation showed pancreatic necrosis that presented as an abscess lateral to the ascending colon. In this Clinicopathological Conference, Dr. Marshall K. Bartlett[2] discussed such a case about four years ago. He had knowledge of still another one that presented as a left psoas abscess. I think this condition has to be distinguished clinically from the pseudocyst of the pancreas that has become infected. This is pancreatic necrosis with or without bacteria.

DR. CASTLEMAN: On its way to becoming a pseudocyst.

DR. QUINBY: But it presents as an inflammatory mass first.

DR. CASTLEMAN: Did Dr. Coe not drain a great deal of fluid from this?

DR. QUINBY: Yes; he did, but the "fluid" was not thin pancreatic secretion. It looked just like very thick pus with necrotic solid particles in it that may have represented fat necrosis or particles of necrotic pancreas itself. The patient improved dramatically, was able to eat and has done well since. The patient operated on two weeks previously, who had practically the same condition, has been fairly well since the necrotic material in the pancreas was drained. His drainage sites have virtually healed. However, he still has upper abdominal complaints similar to those before the recent operation and for which he had had various operations elsewhere. Perhaps he will get some relief for the chronic pancreatitis by operative division of the sphincter of Oddi, as advocated by Doubilet and Mulholland.[3]

DR. STOKES: How did the liver and gall bladder appear?

DR. QUINBY: I do not believe that I remember the liver specifically. It was not biopsied. A cholecystostomy was done, but no stones were found in the gall bladder.

REFERENCES

1. Brilhart, K. B., and Priestley, J. T. Pseudocysts of pancreas. *Am. J. Surg.* **81**:151-160, 1951.
2. Case Records of the Massachusetts General Hospital (Case 37421). *New Eng. J. Med.* **245**:614-618, 1951.
3. Doubilet, H., and Mulholland, J. H. Surgical treatment of recurrent acute pancreatitis by endocholedochal sphincterotomy. *Surg., Gynec. & Obst.* **86**:295-306, 1948.

CASE 42062

PRESENTATION OF CASE

A sixty-seven-year-old woman was admitted to the hospital in semicoma.

At least ten years previously she began to exhibit irritability and stubbornness. She gradually became unable to manage her affairs. Approximately ten years before entry she began to have difficulty walking. The gait was wide-based, was markedly unsteady and became progressively worse. Memory impairment, especially for recent events, became evident seven or eight years before admission, and subsequently became quite marked. Speech difficulty characterized by slurring and impaired articulation appeared approximately three years before admission. Eventually, she was almost impossible to understand. By contrast she appeared to understand most of what was said to her. About three years before admission she began to have difficulty in using the arms and hands. The hands became very unsteady, and the arms were engaged in ceaseless involuntary movements. As a consequence it became quite difficult for her to feed herself or to perform other tasks requiring the use of the hands. Approximately three weeks before admission she fell down a number of stairs and was unconscious for about ten minutes. She recovered satisfactorily from this, and according to the family regained her previous status. One week later she again fell downstairs, and did not respond for several minutes. When she regained consciousness she exhibited little awareness of what was going on about her, and her speech was less intelligible than usual. She also seemed less able to understand what was said to her. There was no evidence of paralysis, however, and she was able to be up and about. On the day before admission she fell for a third time, and thereafter she was confined to bed and remained in a state of stupor. Because of this deterioration in her general condition she was hospitalized.

She had had many falls over the years since the onset of the gait difficulty. There was no history of mental impairment after any of these earlier falls. However, during one of them, she fractured the right humerus and had had some difficulty in using the right arm since that time. Except for her neurologic disorder, her general health had been good. She was admitted to another hospital for study of the nervous disorder about seven years before admission, when physical examination revealed a blood pressure of 150 systolic, 80 diastolic. Cranial-nerve function was normal except for a paucity of facial expressiveness. Constant movements, apparently purposeless, were noted in the arms and face. She walked with a wide base, and there was loss of the normal associated movements of the arms. There was moderate increase in tone upon passive motion of all limbs. Movements of the limbs were free and strong except for the right arm, which was somewhat atrophic and weak presumably because of a fixation of the right shoulder. The tendon reflexes were hyperactive and symmetrical; plantar reflexes were flexor. No sensory abnormality was detected. Further testing of mental function disclosed a disorientation as to time and place, and a loss of memory for recent events. Simple arithmetical tests could not be performed. Knowledge of current events was very poor. There was no evidence of aphasia. Films of the right shoulder showed an impacted fracture of the surgical neck of the humerus. X-ray films of the skull were said to be normal except for a curved line of opacity lying to the left of the sella turcica. An electroencephalogram showed diffuse slow waves, which were more marked on the right side. A diagnosis of cerebral arteriosclerosis was made.

There was no family history of neurologic disease. The patient's mother had died at fifty-five and her father at eighty years of age. A half-brother and half-sister were said to be living and well. The patient had two children, who were in good health.

Physical examination at the time of admission to this hospital revealed a poorly responsive, thin, dehydrated woman. She responded to painful stimuli by occasional avoidance movements, and there was frequent moaning; she did not respond to verbal

commands or make an attempt to speak. There was a small, slightly elevated ecchymosis on the right forehead. The conjunctiva of the right eye was slightly injected. The other positive findings were confined to the neurologic examination. Painful stimuli of the limbs evoked withdrawal movements, and in addition, the patient exhibited occasional brief movements of flexion or extension of different parts of the extremities. At other times a variety of continuous, apparently involuntary, movements were seen in the hands. There were no abnormalities of cranial-nerve function. The tendon reflexes were +++ on the left side and ++ on the right. There was a Babinski reflex on the left.

The temperature was 99.6°F. by rectum, the pulse 88, and the respirations 24. The blood pressure was 90 systolic, 70 diastolic.

Examination of the blood revealed a hemoglobin of 12.2 gm. per 100 ml. and a white-cell count of 25,700. The sodium was 160 milliequiv., the chloride 127 milliequiv., the potassium 4.5 milliequiv., and the carbon dioxide combining power 18 milliequiv. per liter. The nonprotein nitrogen was 160 mg. per 100 ml. On lumbar puncture no measurable pressure was obtained. The cerebrospinal fluid was xanthochromic, with a protein of 450 mg. per 100 ml. There were 3330 fresh red cells per cubic millimeter that were thought to have resulted from the traumatic puncture. An electrocardiogram taken several hours after admission, when the pulse rate had risen to 180 per minute, revealed atrial flutter with a 2:1 block. X-ray films of the skull showed no evidence of a fracture. There was a questionable shift of a calcified pineal gland to the left.

Several hours after admission, an operation was performed.

Differential Diagnosis

Dr. Vincent P. Perlo*: The patient had a progressive neurologic illness of at least ten years' duration and more recent symptoms for three weeks before hospitalization. It appears likely that she had two neurologic diseases, the first of many years' duration and the second evolving over a period of weeks. The two conditions were probably related indirectly.

At about the age of fifty-seven there was a change in the patient's personality described as irritability and stubbornness. Within a few years, in addition to these changes in the emotional sphere, evidence of severe organic dementia appeared. The picture of impaired recent memory, disorientation and restricted fund of knowledge without any aphasic disorder is what one finds in organic dementia. The disturbance of intellectual function indicated diffuse cortical damage, mainly involving the frontal lobes. Shortly after the mental symptoms appeared other neurologic abnormalities were noted. These included unsteadiness of gait and, later, dysarthria and incoordination of the hands. A prominent manifestation was a movement disorder with purposeless, constant, involuntary movements of the arms and face. From the description in the protocol, these movements can be characterized as choreiform. A few years after the onset of symptoms the patient was hospitalized and at that time demonstrated clear-cut neurologic abnormalities, including mental deterioration, expressionless facies, involuntary movements of arms and face, resistance to passive motion of the limbs and a broad-based gait. At that time, the reflexes were rather brisk, but the plantar responses were flexor. No sensory impairment or cranial-nerve abnormality was noted.

About the localization of the pathologic process responsible for the symptoms, it is obvious that disease of the cerebral cortex alone could not account for all the neurologic findings. Diffuse cortical damage involving primarily the frontal lobes was reflected in the organic dementia and the early symptoms of irritability and stubbornness. The lack of facial expression, the movement disorder, the increased tone and the lack of associated movements in the extremities were manifestations of extrapyramidal disorder and indicated involvement of the basal ganglions. The apparent preservation of motor power without pathologic reflexes indicated fairly good function of the pyramidal system. Sparing of long sensory tracts was also evident, and there was no cranial-nerve involvement, which one would expect in a disorder affecting brain-stem structures. Thus, the anatomical localization seemed to involve cortex and basal ganglions.

There was no indication of any space-occupying lesion until a few weeks before hospitalization. Seven years before admission x-ray films of the skull were not remarkable except for a curved line adjacent to the sella turcica, which was most probably calcification in one of the carotid arteries. At that time an electroencephalogram showed diffuse slow-wave activity without any definite focal abnormality. One might argue the case for a slowly growing tumor that finally resulted in the rapid development of symptoms leading to the most recent hospitalization. Can tumor be safely excluded? Although it is true that certain infiltrating tumors, especially oligodendroglioma and slowly growing astrocytoma, may produce neurologic signs for a period of years, it would be most unusual not to find evidence of increased intracranial pressure before ten years of tumor growth. Meningioma, another slowly growing tumor, could hardly have resulted in the diffuse neurologic signs that the patient had. Another point against tumor is that rarely, if ever, do tumors invading the basal ganglions result in the type of movement disorder that this patient had. There was no evidence of an inflammatory process and no stigmas of central-nervous-system syphilis—one can assume that the spinal fluid was examined seven years before admission and was not remarkable. Any of the usual types of vascular disease of the brain resulting in cerebral infarction can be excluded by the slowly progressive course without the

*Assistant neurologist, Massachusetts General Hospital.

suggestion, until just before hospitalization, of any acutely developing symptoms. Infarction of the brain results in abruptly developing signs and symptoms, and certainly there was no acute episode in this case over a ten-year period.

One must therefore conclude that the ten-year illness represented some type of chronic degenerative disease involving cortex and basal ganglions. The presenile dementias, Pick's disease and Alzheimer's disease, must be mentioned although these conditions are characterized predominantly by severe dementia without any striking extrapyramidal features. The chronic progressive form of multiple sclerosis is seen rather more frequently than is usually taught. However, the age at onset in this case is against multiple sclerosis, and the lack of cranial-nerve involvement or pyramidal-tract disturbance safely excludes it. Schilder's disease must be mentioned, but rarely occurs in this age group and almost always is manifested by severe visual disturbance and signs of pyramidal-tract damage.

The one condition that best fits the clinical picture in this case is Huntington's chorea. This illness is characterized by slowly progressive dementia associated with a characteristic movement disorder. Actually, the syndrome of dementia and adult chorea is almost specific although it is believed by some that the entity of senile chorea does exist as a separate condition. The major drawback to the diagnosis of Huntington's chorea is the absence of a family history. However, sporadic cases appear, and initial symptoms may begin in the fifth or sixth decades. The patient showed a classic picture of Huntington's chorea. The first symptoms were in the emotional sphere. Later, dementia, choreiform movements, ataxia and other signs of extrapyramidal disorder appeared. The electroencephalogram obtained seven years before admission was similar to that described in other cases of Huntington's chorea.

The events leading to hospitalization seem fairly obvious. Three weeks before admission the patient fell, apparently because of the unsteadiness caused by her chronic neurologic disease. A week later she fell again—a likely possibility is that this fall was the result of damage sustained in the fall one week before. The third fall resulted in stupor and the picture on admission. The blood chemical levels described are consistent with dehydration and possibly underlying kidney disease. An x-ray film of the skull showed no fracture. This sequence of events in an elderly person suggests the diagnosis of subdural hematoma, probably developing after the initial injury three weeks before admission and perhaps causing the subsequent falls. Epidural hemorrhage in the absence of skull fracture is unlikely. Intracerebral clot on a traumatic basis would have produced a hemiparesis and deeper stupor than the patient manifested at the time of admission. The xanthochromic spinal fluid containing a high protein and some red cells is consistent with a subdural hematoma of three weeks' duration and also some fresh bleeding into the subarachnoid space. I assume that the operation performed several hours after admission was a trephination over the right temporal area to look for a subdural hematoma. The right-sided localization of the hematoma was indicated by the pyramidal-tract signs on the left and a shift of the pineal gland to the left.

Clinical Diagnoses

Chronic degenerative brain disease.
?Subacute hematoma.
Pneumonia, left lower lobe.

Dr. Vincent P. Perlo's Diagnoses

Huntington's chorea.
Subdural hematoma, right frontotemporal.

Anatomical Diagnoses

Huntington's chorea.
Subdural hygroma, with formation of neomembranes, bilateral.

Pathological Discussion

Dr. Salomon Hakim: The patient was explored through bilateral burr holes. A heavily xanthochromic fluid was encountered in the subdural space over both cerebral hemispheres. The pia appeared slightly thickened and was separated from the dura by 2 cm. For two days postoperatively the patient was given Cedilanid, 0.8 mg., with relief of the paroxysmal tachycardia. She remained unconscious and died quietly in progressively deepening coma on the twenty-sixth hospital day.

At autopsy when the dura mater was opened about 250 ml. of clear, yellowish fluid was encountered in the subdural space over the convexity of the hemispheres. The entire subdural space of the brain was lined by a very thin, translucent membrane, which, over the convex surfaces of the hemispheres and symmetrically on both sides, consisted of distinct inner and outer membranes between which was the subdural fluid. These membranes were adherent neither to the dura nor to the arachnoid (Fig. 1). The brain, including the brain stem and cerebellum, weighed 1360 gm.

Neuropathological examination showed the presence of a diffuse chronic degenerative disease of nerve cells, in which the neurons of certain regions were much more severely affected than those elsewhere. Particularly striking was the severe degeneration and atrophy of the caudate nucleus and putamen, considerably more pronounced in the former than in the latter (Fig. 2). In these nuclear masses the large neurons had been relatively spared, whereas the small nerve cells had almost entirely disappeared. Moreover, all portions of the forebrain showed neuronal degeneration to some degree, as well as the thalamus and the globus pallidus. The brain-stem structures were relatively intact, and the cerebellum showed only

a minor degree of Purkinje-cell loss, which cannot be considered specific.

These findings are typically those of Huntington's chorea, in which disproportionate atrophy of the

FIGURE 1. *Photograph, Showing the Dura* (A) *and the Outer* (B) *and Inner* (C) *Neomembranes. The arachnoid* (D) *is normally covering the brain.*

caudate and putamen are characteristic. The process also affects the cortex of the frontal lobes severely and many other parts of the cerebrum and brain stem to a lesser degree. The pathological and clinical aspects of

FIGURE 2. *Coronal Section of the Brain through the Anterior Horns of the Lateral Ventricles and the Anterior Portions of the Lenticular Nuclei.*

Note the severe atrophy of the caudate nuclei with resulting dilatation of lateral ventricles. Contrast with the normal appearance (Fig. 3).

this disease are well reviewed in Wilson's *Neurology*.[1] A typical case presenting much the same problem as the one under discussion was the subject of a clinicopathological conference here in 1943.[2] The strongly hereditary nature of this disorder is universally recognized, and it is of interest that the patients originally described by Huntington in 1872 were descendants of a family that had come to Boston from England in 1630.[3] Many cases continue to appear in New England to this day. Sometimes, however, cases in which there is apparently no hereditary background occur, although the clinical and pathological manifestations are typical. These are probably either sporadic cases or cases in which an accurate family history cannot be obtained, as appears to have been true in the case under discussion.

The pathogenesis of the involuntary movements is not clear. Most of the textbooks of neurology state that the severe degeneration of the striatum (caudate nucleus and putamen) is responsible for the characteristic choreoathetosis. However, the process extends far beyond these structures, so that a precise clinicoanatomical correlation is impossible. The widespread

FIGURE 3. *Coronal Section of a Normal Brain through the Anterior Horns of the Lateral Ventricles and the Anterior Portions of the Lenticular Nuclei.*

neuronal degeneration in the cerebrum and diencephalon accounts well for the mental changes.

Because of the involuntary movements, these patients often fall down, and are therefore disposed to head injury. Subdural hematoma is thus a frequent complication. In this case, there were bilateral subdural hygromas, which may also result from cranial injury. It is assumed that in the formation of subdural hygroma, a traumatic tear in the arachnoidal membrane results in escape of cerebrospinal fluid into the subdural space. Because of a valvelike action of the tear in the arachnoid, the subdural cerebrospinal fluid is unable to return to the subarachnoid space.[4] This series of events seems to have occurred in the case under discussion.

REFERENCES

1. Wilson, S. A. K. *Neurology*. 1838 pp. Baltimore: Williams & Wilkins, 1940. Pp. 844-857.
2. Case Records of the Massachusetts General Hospital (Case 29072). *New Eng. J. Med.* **228**:233-235, 1943.
3. Vessie, P. R. On transmission of Huntington's chorea for 300 years — Bures family group. *J. Nerv. & Ment. Dis.* **76**:553-573, 1932.
4. Dandy, W. E. Brain. In *Practice of Surgery: Clinical, diagnostic, operative, postoperative*. Edited by D. Lewis, et al. Vol. 12, Chapter I. Hagerstown: Prior, 1932. Pp. 306-310.

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PHYSICIAN AND PHARMACIST

BETWEEN 1901 and 1917 Massachusetts adopted certain "pure food and drug" laws, among them Section 187 of Chapter 94 of the *General Laws*, which defined and penalized the misbranding of foods and patent medicines and also prescribed the manner of labeling such products. False statements were made illegal, and any content of potentially harmful drugs (such as opium and acetanilid) had to be indicated on the label so that the purchaser would be warned.

Section 187 was improved and amended in 1948, a sentence being included to the effect that the labeling provisions should not apply to the compounding and dispensing of drugs "on the written prescription" of a physician, dentist or veterinarian. (Presumably, this was intended to save the druggist time and trouble, and assumed that prescriptions would not be likely to be written for adulterated or harmful preparations, or false claims made concerning them.) A section 187a was also added in 1948, providing that "no person shall sell or offer for sale at retail, or dispense or give away any harmful drugs . . . . to any person other than a physician, ... *except on a written prescription* of a physician . . . ." "Harmful" drugs were specified by name.

By 1953 it was realized that nothing in the law prohibited a person from selling harmful drugs on the *oral* prescription of a physician, and with the thought that the distribution of "goof balls" (barbiturates and amphetamine), to which much juvenile delinquency was attributed, might be controlled more effectively, it was proposed that the term "oral or written prescription" should be used. An effort was also made to distinguish "harmful" from "dangerous" drugs, and a provision was included that "no person shall dispense *any drug* either on oral or written prescription, in a container that did not bear a label *with the name and address of the druggist.*" This provision (perhaps innocently) assumed that no one ever bought or should buy drugs except from a drugstore, and it ignored the common practice in rural areas whereby physicians dispense and sell their own pills without benefit of pharmacies. The bill did not pass, but in 1954 a modified version was enacted. This is the controversial Chapter 577 of 1954. It again revises Section 187 and Section 187a, and defines in detail the meaning of "oral prescription" and "written prescription." The "oral prescription," after being verbally transmitted to the pharmacist, must be at once reported by him on a form containing among other things the name and address of the prescriber, the *name of the pharmacist,* the name of the *patient,* directions and cautionary statements, and the number of times to be refilled. The written prescription must also contain the name of the patient, cautionary statements and the number of times to be refilled—matters that physicians are not ordinarily accustomed to include in their prescriptions.

Nowhere does Chapter 577 make any provision for the dispensing or the sale of drugs directly to patients by the physician; indeed the new law expressly states that "no person shall sell or offer for sale at retail or dispense or give away any harmful drug to any person other than a physician," except on oral or written prescription and, even more broadly (though perhaps again inadvertently), omits the word "harmful" in adding that "no person shall dispense any drug upon an oral or written prescription in a container which does not bear a label *which gives the name and address of the druggist.*"

The right of the physician to administer "harmful" drugs was preserved, apparently as a hasty afterthought, in a subsequent paragraph whose wording was agreed upon by representatives of the Massachusetts Medical Society. This provides that "a physician . . . . *may personally administer* any harmful drug."

This law, now in effect, is being administered and enforced by the Food and Drug Division of the Department of Public Health and the Board of Registration in Pharmacy, which employs an investigator to visit physicians' offices to see what stocks of drugs they maintain and whether they are selling them. The law carries a penalty of $1,000 or a jail sentence of one year or both for its violation.

The representative of the Department of Public Health has stated that he will not prosecute physicians for minor offenses such as selling or dispensing small amounts of drugs because he does not think the courts will uphold him, but that he intends if he can to put physicians who maintain private dispensaries or large stocks of drugs out of business.

The only proposed corrections thus far offered are contained in a bill (House 1179) to modify the words "no person shall dispense any drug" to "no person shall dispense any *harmful* drug," and to change the wording that a physician "may personally administer" to "shall be personally responsible" for the administration of harmful drugs.

It has been held that the law as written and passed deliberately omitted the words "harmful" in the paragraph cited, thus making it illegal for a physician to dispense or sell any drugs. The representative of the Division of Food and Drugs is inclined to agree with this interpretation. Others deny that the omission of the word "harmful" was intentional, and point out that the whole purpose of the law is to control the distribution of *harmful* drugs (such as amphetamine and barbiturates) — not to destroy the custom of dispensing ordinary drugs by physicians.

However, the pharmacists have only too readily pointed out that no doctor should be permitted to sell drugs to his patients, even though he may sell them better drugs at lower prices than the drugstore, since this is a violation of fair-trade practice and interferes with what they consider their normal right — a monopoly on selling drugs.

Thus, bad feelings have arisen, and the matter is in danger of turning into a squabble over mercantile rights, rather than a sincere attempt to help the Department of Public Health in its campaign against the uncontrolled distribution of potent drugs to irresponsible "addicts" and delinquents.

HOSPITAL SURVEY AND CONSTRUCTION PROGRAM AND ITS AMENDMENTS

On November 22, 1955, the Massachusetts Department of Public Health held a public hearing to present the details of the Seventh Revision of the Massachusetts State Plan for the Administration of Public Law 725.

Since 1948, the Department of Public Health has allocated approximately $15,000,000 in federal funds for the construction of hospitals and health centers within the Commonwealth. Dr. A. Daniel Rubenstein, director of the Division of Hospital Facilities of the Department, has summarized this program in the *Journal.** It is apparent that the Department of Public Health has made equitable distribution of funds among the hospitals of the Commonwealth. It is gratifying to realize that a governmentally sponsored program of this type is being carried on under the existing pattern of medical care with a high degree of efficiency.

Each year the State plan must be revised to develop the necessary priority scheme according to which grants are made to hospitals. Special grants for particular problems are also incorporated in the plan. In Massachusetts, for example, special classifications of aid have been set up to improve maternity departments in hospitals and also to help teaching hospitals establish better facilities to improve the teaching of interns and residents.

This year, for the first time, the State plan includes a survey of nursing homes, outpatient facilities and rehabilitation centers. As Dr. Rubenstein explained at the hearing, this was the first step in carrying out the requirements of the Wolverton amendment to the Hospital Survey and Construction Act (Hill–Burton program), which makes available federal funds for the three groups mentioned above, in addition to chronic-disease hospitals. Priorities were distributed at the hearing to indicate which communities had prior demand on federal funds, in accordance with the survey.

The potential impact of an extensive construction program, such as this, on facilities for medical care in Massachusetts is far-reaching. In a well administered program, federal aid will do more than provide more health facilities for more people. It is hoped that by proper co-ordination of services and efficient integration of facilities, all facets of medical

*Hospital survey and construction program in Massachusetts: five-year study. *New Eng. J. Med.* **251**:177-183, 1954.

care will be made available at a lower over-all cost. It is expected that the concept of regionalization will be extended so that duplication of services throughout the State will be reduced as much as possible. In the field of rehabilitation, for example, the Department is recommending that no more than three, or possibly four, well developed rehabilitation centers be planned for the State. Here, again, this is long-range planning with the realization that personnel, trained in rehabilitation, is not readily available so that progress in this field may not be too rapid. To help the Department develop its medical-care plan under this program, the Hospital Advisory Committee, made up of experts, able physicians, administrators and community leaders, has been appointed by the Governor. The Department of Public Health, working with this committee, has demonstrated that Government support may be made available under the present system of free enterprise to the mutual advantage of patients and physicians. It is hoped that this excellent program, whose potential contribution to health is enormous, will be carried on as efficiently in the future as it has been in the past.

MEDICAL RESEARCH: A MIDCENTURY SURVEY

THE American Foundation, established in 1924 by Edward Bok, primarily for the finding of facts and the relating of them, one to another, has completed a fifteen-year study of basic research in medicine. The results have been embodied in a comprehensive two-volume report, "lucid enough for the layman and detailed enough for the scientist." Prepared under the supervision of a committee of 26 eminent consultants from material submitted by universities and medical schools, hospitals, foundations, research institutes, industries and governmental departments, it has been published for the Foundation by Little, Brown and Company, of Boston. Esther Everett Lape is the Foundation's member in charge; the consultants include both fundamental scientists and clinicians.

The thesis on which *Medical Research: A mid-century survey* is based is that the greatest hope of solving the nation's — and the world's — outstanding medical problems "lies in fundamental research in laboratories of biology, chemistry, physics, atomic energy." The first volume, accordingly, is on American medical research in principle and practice; the second on unsolved clinical problems in biologic perspective. They are addressed to all who are interested in scientific medical care, whether on the dispensing or the receiving end of the line.

In the various chapters such problems are discussed as the pertinence of the structure of the protein molecule to the progress of medicine, for it has been estimated that some 100,000 different proteins in the human body exercise their specific effects on biologic activity. Mathematics itself, the most abstract of the sciences, figures increasingly in medical research, even through the mysteries of the mechanical brain; if perfection in this particular can be surpassed it must lie in the possibility, which has been presented, of constructing a brain capable of making human mistakes! In relation to mathematics and its solid impact on the world within us is the study of cybernetics, the science of communication and control based largely on the principle of feedback. According to this engaging philosophy "action in response to an input of information includes the results of that action in the new influence by which subsequent behavior is modified." According to one authority, cybernetics offers an unusual opportunity of opening the way for the control of functional psychoses.

When one considers the labor of producing these volumes as a co-ordinated, directed effort, they are seen to constitute a synapse between the faultless concepts of pure science and the immediate service to which the practice of medicine is dedicated. More than this, they provide abundant evidence that medicine itself is on the way to becoming an exact science — always within the boundaries, one may believe, of the humanizing ideal that is its art.

NEW MEDICAL SCHOOL PROPOSED

THE general intensified interest in the quality and character of medical education and the financial considerations that are inseparable from it has had its repercussions also in the Orange Free State, so-called, and the Transvaal, according to a recent *Boston Herald–New York Times* dispatch from Johannesburg. The dispatch had at the time freshly emanated from a convention of African witch doctors currently assembled in Pretoria.

There may be, of course, those who are inclined to take not too seriously a modern analogue of the aboriginal witch medicine that has held such power over the minds and bodies of men since first they walked erect. This great and ancient culture need not be lightly brushed aside, however, by a profession that, within the memory of those still living, has bled and puked and plastered, applied the leech, scoured the bowels and loosened the teeth with heavy metallic poisons and coaxed its patients' ills away with infinite dilutions of the like that cures like, reduced to the vanishing point. For the modern African witch doctor, versed in the use of natural herbs and similar simple remedies, gives no acknowledged credence to voodoo; nor does he openly invoke the magic formulas once considered sacred to his practice and still not entirely foreign to that of many a modern white man's pseudoprofessional cult.

One of the problems discussed, in fact, by the native medicine men who had come to the convention from Zululand, Basutoland and Swaziland,

among other provinces, was the elimination of quacks who cure by incantation. The conservative members of the "regular" school of therapy want the government to recognize them as herbalists and herbalists alone.

In line with this policy the witch doctors, organized as the African Dingaka Association, contemplate the raising of $30,000 — a not excessive sum, according to modern standards — for the establishment of a five-year medical college on land already owned by the Association in Pretoria. Such use of the land, however, might be prevented by operation of the government's group areas act, which specifies where in Africa Africans may dwell.

An extra requirement for graduation from the school, in addition to passing an examination in diagnosis and herb treatment, would be the ability to read and write. The last qualification, of special importance, resulted from the inspection and attempted interpretation of a number of white doctors' prescriptions.

Schools for witch doctors are in operation in other parts of Africa, such as North Nyasaland, although the time-honored system of apprenticeship is the usual method by which these practitioners obtain their technical training.

Dr. Southwood Smith has been giving a very important series of lectures in Edinburgh, on the subject of epidemics. Dr. Smith dwelt particularly, in his introductory lecture, on the fact that all epidemic diseases — the plague, black-death, sweating-sickness, cholera, influenza, &c., were fevers. Cholera was usually preceded, he stated, by influenza. — Dublin Med. Press.

Boston M. & S. J., *February 14, 1856*

MASSACHUSETTS MEDICAL SOCIETY

THE PROBLEM OF MEDICAL LEGISLATION

Not a year goes by but in the grist of more than three thousand bills introduced into the Massachusetts State Legislature there are at least half a dozen, and sometimes many more, that are of great import not only to the practice of medicine but also to the health of the citizens of the Commonwealth. Constant efforts are made by paramedical practitioners to extend their sphere of activity without medical supervision or to restrict the freedom of physicians, and the lunatic fringe is always well represented by bills to hamstring medical research or to make illegal desirable public-health measures.

The Massachusetts Medical Society is obligated to keep an eye on these bills, and to help the Legislature to decide their fate wisely in the best interest of the public. This has been the traditional function of the Committee on State Legislation.

But the Committee on State Legislation is made up of practitioners, unskilled in the interpretation of trickily worded proposals, and can easily overlook important and far-reaching phrases. Often these things are caught in time by some eagle-eyed expert — perhaps only, however, on the eve, or even the morning, of a public hearing at the State House; sometimes they are not detected until too late.

The Committee is ably assisted by Mr. Charles Dunn, legislative counsel, who has served it well in the past and is in a position to carry the opinions of the Society to influential legislators in a more effective way than is possible even in public hearings. But Mr. Dunn is not a physician, and certain nuances of meaning, the medical significance of which is only too apparent (once they have been pointed out) to the physician, may escape the trained lawyer unless he has been alerted by a medical expert.

No easy solution suggests itself. It would be ideal if we could command the services of a medical legal specialist who could promptly obtain and meticulously read every bill of medical import, and fully advise both the Committee and Mr. Dunn. Such an expert (and very few lawyers with medical degrees or physicians with legal training are to be found) would be well worth a sum that would go far toward wiping out the annual surplus of the Society that seems to worry so many of our members.

ROBERT W. BUCK, M.D.
Secretary

COMMITTEE ON MATERNAL WELFARE

PLACENTA PRAEVIA WITH HEMORRHAGE

A thirty-eight-year-old gravida II, para I, was first admitted to the hospital at twenty-nine weeks, because of painless vaginal bleeding. Pregnancy had been uneventful to date, a previous pregnancy having terminated normally at term with the birth of an infant weighing 3.8 kg. (8½ pounds). The patient was given three transfusions during a week in the hospital.

X-ray examination disclosed "a shadow in the anterior portion of the uterus that is quite likely placenta, with no evidence of placenta praevia." No vaginal examination was done. The bleeding gradually stopped after bed rest, and the patient was discharged.

She was readmitted to the hospital six days later (when thirty-one weeks pregnant) because of recurrent painless bleeding. Active labor began en route to the hospital. A double setup was ordered, and a consultant called. He arrived within 10 minutes. His note is paraphrased as follows:

Double-setup examination in the operating room revealed a central placenta praevia and a thin rim (0.9 cm.) of cervix. Three methods of delivering the patient were considered and discussed. The first was to wait for further descent of the vertex. In view of the fact that she was actively bleeding and the fetal heart beat was altered, this method was rejected. Secondly, because the cervix was almost completely effaced and a hand could easily be introduced through it and because the baby was small, the membranes intact with an average amount of amniotic fluid, the head unengaged and movable, and the pelvis roomy, with good soft-tissue elasticity, it was thought that an internal podalic version and extraction could be easily and quickly performed. The third alternative was cesarean section.

It was recognized that version would necessitate going through the placenta. However, the same objection would also have applied to a lower-segment cesarean section. Actually, internal podalic version was selected. It was performed rapidly and without apparent undue bleeding. Both feet were brought down with ease, the trunk extracted, and the aftercoming head delivered easily. Immediately, the baby was given to an assistant while the operator reintroduced his hand and extracted the secundines in toto. Immediately thereafter, there was a gush of amniotic fluid tinged with blood. There was a 1.9-cm. laceration of the posterior lip of the cervix that extended upward into the endometrium for perhaps 1 cm. but did not involve muscular layers. This rent also included a small tear in the vaginal mucosa. There was no pronounced bleeding, and the tear was easily repaired. The entire procedure of version and extraction was timed at thirty seconds on the anesthetist's chart.

At this time the patient went into practically instantaneous, complete collapse and died without warning to the physician anesthetist, who could not subsequently state whether the heart beat or the respirations had stopped first. In fact, he thought that they had stopped simultaneously without prior alteration in either.

The infant, who weighed 2.7 kg. (6 pounds) died in four and a half hours in spite of a transfusion.

Autopsy showed the lacerations described, with evidence of hemorrhage from placenta praevia, but was otherwise negative.

This case was classified as a preventable death from hemorrhage, complicated by severe shock resulting from the trauma of a version and extraction performed through the not quite fully dilated cervix. Despite the consummate skill with which this procedure was carried out and recognition of the reasoning that led to its election, it is believed that no pelvic delivery is justified in the presence of a central or almost central placenta praevia. Previous bleeding had been well treated by the transfusions noted, but, as in most similar cases, the volume of blood lost was probably grossly underestimated and it is likely that transfusions failed to bring the hematocrit and hemoglobin up to safe levels. Since there had undoubtedly been additional copious bleeding immediately before intervention, one may assume that the total blood loss superimposed upon a poor hemoglobin level could easily have plunged the patient into sudden irreversible shock even without the notorious trauma of accouchement forcé. This combination would certainly not respond to transfusion or to the usual emergency measures.

With all the advantage of hindsight, other comments should be made. In the first place it seems regrettable that the x-ray diagnosis of "no evidence of placenta praevia" was relied upon. Secondly, it was courageous, to say the least, to allow the patient to go home, whatever her diagnosis may have been, after a hospital admission in which three transfusions were required late in pregnancy. Nevertheless, she returned in ample time for a double-setup examination, but there is no note of additional transfusions during the double setup, and this is to be deplored.

Finally, the reasoning that a lower-segment cesarean section would encounter the placenta with comparable bleeding is irrelevant, since *classic* cesarean section is the procedure of choice with placenta praevia. The "primary avoidable factor" in this case was considered to be the wrong choice of treatment, involving poor obstetric judgment; there was unanimous opinion that a classic cesarean section should have been performed.

JOHN FIGGIS JEWETT, M.D.
Chairman

CORRESPONDENCE

THE EYES HAVE IT

To the Editor: Serendipity[1] has achieved frequent usage in medical and lay literature of late. I was hopeful that I would have an experience that could be described by this term, and lo! it came to pass.

I have been collecting pleonasms[2] for years but recently lost the book in which my collector's items had been recorded. Deploring this loss, at my desk one day, my eye[3] spotted a copy of the *New England Journal of Medicine* lying casually on my desk.[2] This is the way the *Journal* usually lies (on my desk). Seeking solace, I picked up the *Journal* and by chance opened it at page 666 of the issue of October 13, 1955. In the second column in a letter "To the Editor," paragraph 5, line 4, I found a perfect pleonasm.[4]

My yearning to have an experience, accurately described as serendipity, had been gratified.

LLEWELLYN SALE, M.D.
St. Louis, Missouri

1. A pleasant but unexpected experience.
2. A redundant word or expression.
3. Antecedent of deploring.
4. "The profound myocardial depressant action of ether on the myocardium" and so forth.

CONGRESSES ON BLOOD TRANSFUSION, BLOOD BANKS AND HEMATOLOGY

The International Society of Blood Transfusion and the International Society of Hematology, realizing the overlapping of interest in the fields of hematology and blood transfusion and the number of persons who will wish to attend meetings of both societies, have agreed to hold the Sixth Congress of the International Society of Blood Transfusion and the Sixth Congress of the International Society of Hematology jointly and consecutively in Boston, Massachusetts, in August and September. In addition, the American Association of Blood Banks will become a joint sponsor and hold its annual meeting together with the International Transfusion Congress. The Association will give its full cooperation in the preparation of the scientific program and in the planning of exhibits. Arrangements will be made to

hold the usual administrative and technical sessions of the Association during the course of the Congress. The Sixth International Transfusion Congress and the American Association of Blood Banks will meet jointly from September 3 through September 5. The Sixth International Hematology Congress will meet from August 27 through September 1.

Joint programs of the two congresses are scheduled for September 1 and 3.

Headquarters of both congresses and the site of all the meetings and exhibits will be the Hotel Somerset, Boston. Six hundred rooms have been allotted to the congresses in this hotel and in others immediately adjacent, and a number of inexpensive "dormitory-type" rooms will also be available.

All communications for the Blood Transfusion Congress should be addressed to the Sixth International Congress of Blood Transfusion, Dr. M. H. Sloan, Secretary, 2101 Constitution Avenue, N.W., Washington 25, D.C.

All communications for the American Association of Blood Banks should be addressed to American Association of Blood Banks, Miss Marjorie Saunders, Secretary, 3707 Gaston Avenue, Dallas, Texas.

All communications for the Hematology Congress should be addressed to the International Society of Hematology, New England Medical Center, Harrison Avenue at Bennet Street, Boston 11, Massachusetts.

To facilitate the entrance of foreign members and their families to the United States, the Congress will come under the exchange-visitor program of the State Department. The consulates in the various countries will be notified by the State Department regarding the Congress, which has serial number P-2140, and regarding the Congressists who have been "invited" to attend. This will require an immediate statement that one is planning to attend the Congress. In turn, prospective visitors will be notified that they have been selected to participate in the program. It is *imperative therefore that foreign members immediately send a statement that they will be present, even if this is uncertain.* Every effort will be made to see that all foreign delegates are admitted to the United States with a minimum of difficulty.

The officers of the Sixth Congress of the International Society of Blood Transfusion are as follows: I. S. Ravdin, president (Philadelphia, Pennsylvania); Louis K. Diamond, vice-president (Boston, Massachusetts); Margaret H. Sloan, secretary (Washington, D.C.); Robert F. Norris, treasurer (Philadelphia, Pennsylvania); and Brooke Roberts, assistant secretary (Philadelphia, Pennsylvania).

The officers of the American Association of Blood Banks are as follows: James J. Griffitts, president (Miami, Florida); Ralph Hartwell, vice-president (New Orleans, Louisiana); Marjorie Saunders, secretary (Dallas, Texas); Bernice M. Hemphill, treasurer (San Francisco, California); E. E. Muirhead, president-elect (Dallas, Texas); and Merlin L. Trumbull, immediate past president (Memphis, Tennessee).

The officers of the Sixth Congress of the International Society of Hematology are as follows: William Dameshek, president (Boston, Massachusetts); William C. Moloney, secretary (Boston, Massachusetts); James L. Tullis, treasurer (Boston, Massachusetts); and A. Richardson Jones, associate secretary (Boston, Massachusetts).

Numerous joint committees have been organized: communications; scientific exhibit; commercial exhibit; hotels and housing; liaison with city, state and governmental officials; program; publicity; registration; special events; national advisory; international advisory; and ladies.

The Congress will have four official languages: English, French, Spanish, and Interlingua, with simultaneous translations of the first three. Interlingua will be used for translating summaries of all papers and other documents.

Those wishing to present papers on any appropriate themes should send abstracts of 300 words or less in English, French or Spanish. Abstracts of all papers will be published in Interlingua. Selections of papers will be based on their originality, interest and scientific importance. Papers for the plenary sessions will be twenty minutes in length, and those for the multiple sessions twelve minutes. There will be strict accounting of time. Well made lantern slides whose words can be read in a large auditorium are almost a necessity in the proper presentation of papers. Standard-size (3¼ x 4 inches), 35-mm. and motion-picture projectors will be provided. The "deadline" for the receipt of abstracts is March 1, 1956.

There will be space for both scientific and commercial exhibits accepted for one or both congresses. Those wishing to present scientific exhibits should send an abstract of their topic, indicate the space required, and specify the congress for which the exhibit is intended. Special forms concerning space will be sent on receipt of such information. Prizes for the best exhibits will be given.

Firms wishing to present commercial exhibits should indicate the congress for which the exhibit is intended, the nature of the exhibit and the amount of space required. Special forms concerning space will be sent on receipt of such information.

TABLE 1. *Tentative Agenda for the Congresses.*

SATURDAY, SEPT. 1	MONDAY, SEPT. 3	TUESDAY, SEPT. 4	WEDNESDAY, SEPT. 5
9 a.m. — 12:30 p.m.:			
Autoimmunohematology	*Clinical Problems*	*Preparation and Preservation*	*Plasma and Plasma Derivatives*
Hemolytic anemias	Transfusion reactions	Blood, separated formed elements and blood derivatives	Fractionation
Autoimmune antibodies of various types	Errors and abuse of blood transfusions		Coagulation factors
	Effects of massive transfusions		Heat-stable preparations
	Use of blood in burns		Plasma-volume expanders
			Properdin
2 — 5:30 p.m.:			
I.	*Hepatitis*	*Anthropology* (if not completed on Monday afternoon)	Organization problems
A. Hemolytic anemia	Incidence		
B. Erythroblastosis	Screening tests	Medicolegal aspects of blood immunology	
	Use of gamma globulin		
II.	Other-disease transmission	Transfusion equipment	
A. Thrombocytopenia	*Isoimmunohematology*	Plastic bags	
B. Leukopenia	New blood groups and antibodies	Reports of blood-transfusion service	
	Anthropology		
	Immunochemistry		

A motion-picture salon will be set up for showing of 16-mm. motion pictures, silent and sound. Those desiring to show motion pictures will send an abstract of their topic.

Special events will be announced later.

A joint travel committee headed by Dr. Morten Grove-Rasmussen has made arrangements for reduced rates of travel by plane and ship. Approximate round-trip cost by plane, Paris-Boston-Paris, will be $325. Further information will be forthcoming. It is essential, however, to make advance reservations now.

Based on the possibility of obtaining grants from pharmaceutical houses, governmental sources and so forth, it will be possible to extend some degree of travel assistance to a limited number of delegates. It is suggested that notification that this type of assistance is desired be submitted to the appropriate secretary.

The Somerset Hotel, where all the meetings will be held, is allotting 300 rooms for the Congress. In addition, 300 rooms have been engaged at nearby hotels. "Dormitory" accommodations at approximately $3 a day will be available either at the hotels or at nearby universities.

An extensive program for ladies is being arranged.

Deadline date for titles and abstracts is March 1, 1956. All communications on this subject should be submitted to the appropriate secretary, as indicated above.

A tentative program is presented in Table 1. This may be altered or rearranged, depending on subject matter and speakers available later.

LOUIS K. DIAMOND, M.D.

Boston

REGARDING LOCAL TETANUS

To the Editor: I read with interest the recent case report entitled "Local Tetanus" in the Medical Intelligence section of the November 3, 1955, issue of the *Journal* by Drs. Peirce and Dabbs. This recalls a case that I reported in the *Archives of Neurology and Psychiatry* (**41**:788-792, 1949). This boy had cephalic tetanus five days after a facial wound, and ipsilateral facial paralysis, with contralateral facial spasm corresponding to the textbook description of cephalic tetanus, developed. The similarity of the photographs of the face in the case reported by Drs. Peirce and Dabbs and in that reported by me suggests that there may also have been some facial paralysis in their case.

In view of the rarity of this condition attention is called to this previous report.

ARTHUR L. WATKINS, M.D.

Boston

RESERPINE IN DERMATOLOGY

To the Editor: On page 238 of my Medical Progress report on dermatologic therapy, published in the August 11, 1955, issue of the *Journal*, in the section on therapy for psoriasis I cited the results of an attempt by Rein and Goodman to evaluate the efficacy of reserpine. Since the point is discussed under this heading it would be readily assumed that the patients treated had psoriasis.

However, Dr. Rein has called my attention to the fact that it was not used in cases of psoriasis. According to the article by Rein and Goodman, because of the tranquilizing qualities of the drug, it was prescribed by them for patients with dermatoses affected by psychogenic or emotional tension factors.

I regret this mis-statement.

J. G. DOWNING, M.D.

Boston

TRACHEAL BUCKLING

To the Editor: A diagnostic feature used to an advantage at our hospital was demonstrated in the presentation of Case 41512 in the December 22, 1955, issue of the *Journal* — an x-ray finding that has served as a fairly reliable differential point between neoplasm and inflammation and would perhaps have allowed a correct preoperative diagnosis. The clue is the position of the trachea, which, as a rule, in our experience, buckles acutely after inflammation and scarring. In the upper portions of the lungs, the specific agent has usually been tuberculosis.

With neoplasm in the region of the right-upper-lobe bronchus, the trachea remains mid-line and may deviate gently but is rarely buckled acutely. These observations have been documented in the *Archives of Otolaryngology* (**57**:44-50, January, 1953) in an article by Poppel et al. entitled "Tracheal Buckling: Differential roentgen sign."

HERBERT S. BERLIN, M.D.
Associate Radiologist
Veterans Administration Hospital

Bronx, New York

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this list must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Bone and Joint X-Ray Diagnosis. By Max Ritvo, M.D., assistant clinical professor of radiology, Harvard Medical School, instructor in radiology, Tufts University School of Medicine, lecturer on radiology, Boston University School of Medicine, director, Department of Radiology, and roentgenologist-in-chief, Boston City Hospital, and associate radiologist, Beth Israel Hospital. 4°, cloth, 752 pp., with 568 illustrations. Philadelphia: Lea and Febiger, 1955. $20.00.

Surgery of the Alimentary Tract. In 3 volumes. By Richard T. Shackelford, M.D., assistant professor of surgery, Johns Hopkins University School of Medicine. Assisted by Hammond J. Dugan, M.D., assistant in surgery, Johns Hopkins University School of Medicine. 4°, cloth. Vol. 1: 862 pp., with 583 illustrations; Vol. 2: 771 pp., with 441 illustrations; Vol. 3: 940 pp., with 681 illustrations. Philadelphia: W. B. Saunders Company, 1955. $60.00 per set.

Erlebtes aus der Thoraxchirurgie. By Prof. Dr. Rudolf Nissen, director, Chirurgische Universitätsklinik, Basel. 4°, paper, 66 pp., with 99 illustrations. Stuttgart: Georg Thieme, 1955. DM 14.40.- $3.40. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Cardiac Auscultation: Including audio-visual principles. By J. Scott Butterworth, M.D., associate professor of medicine, New York University Post-Graduate Medical School; Maurice R. Chassin, M.D., assistant professor of clinical medicine, New York University Post-Graduate Medical School; and Robert McGrath, M.D., associate professor of clinical medicine, New York University Post-Graduate Medical School. 8°, cloth, 111 pp., with 54 illustrations. New York: Grune and Stratton, 1955. $4.50.

Psychology in Nursing. By Wendell W. Cruze, Ph.D., professor of psychology, Wilson Teachers College, visiting lecturer in psychology, Johns Hopkins University School of Medicine, lecturer in psychology, Garfield Memorial Hospital School of Nursing, and lecturer in psychology, Lucy Webb Hayes School of Nursing of Sibley Memorial Hospital. 8°, cloth, 494 pp., with 79 illustrations and 9 tables. New York: Blakiston Division, McGraw-Hill Book Company, Incorporated, 1955. $5.50.

Morbidity in the Municipal Hospitals of the City of New York: Report of an exploratory study in hospital morbidity reporting. By Marta Fraenkel, M.D., assistant to the Commissioner and Director of Medical Statistics and Records Service, Department of Hospitals, City of New York; and Carl L. Erhardt, director, Bureau of Records and Statistics, Department of Health, City of New York. 8°, cloth, 229 pp., with 56 tables. New York: Russell Sage Foundation, 1955. $4.50.

Symposium on Atherosclerosis: Held under the auspices of the Division of Medical Sciences, National Academy of Sciences — National Research Council, at the request of the Human Factors Division, Air Force Directorate of Research and Development, March 22 and 23, 1954. 8°, cloth, 249 pp., with illustrations and tables. Washington, D.C.: National Academy of Sciences — National Research Council, 1954. (Publication No. 338.) $2.00.

Cornell Conferences on Therapy. Vol. 7. Edited by Harry Gold, M.D., managing editor, and David P. Barr, M.D., McKeen Cattell, M.D., Frank Glenn, M.D., and George Reader, M.D. 8°, cloth, 264 pp. New York: Macmillan Company, 1955. $4.50.

Principles of Medical Statistics. By A. Bradford Hill, C.B.E., D.Sc., Ph.D., F.R.S., professor of medical statistics in the University of London (London School of Hygiene and Tropical Medicine). Sixth edition, revised and enlarged. 8°, cloth, 314 pp., with 44 tables. New York: Oxford University Press, 1955. $4.00.

Perinatal Mortality in New York City: Responsible factors: A study of 955 deaths by the subcommittee on neonatal mortality, committee on public health relations, The New York Academy of Medicine. Analyzed and reported by Schuyler G. Kohl, M.S., M.D., Dr. P.H. 8°, cloth, 112 pp., with 67 tables. Cambridge: Harvard University Press, 1955. $2.50. (Published for the Commonwealth Fund.)

Studies on Fertility: Including papers read at the Conference of the Society for the Study of Fertility, London, 1954. (Vol. 6 of the Proceedings of the Society.) Edited by R. G. Harrison, M.A., D.M., Derby Professor of Anatomy, University of Liverpool. 8°, cloth, 151 pp., with illustrations and tables. Springfield, Illinois: Charles C Thomas, 1955. $4.25.

Spirometric and Gas Analytic Studies in Pulmonary Insufficiency at Rest and during Graduated Exercise. Vol. 6 — Supplementum 12. By Teuvo K. I. Larmi. 8°, paper, 166 pp., with 32 illustrations and 9 tables. Helsinki: Scandinavian Journal of Clinical and Laboratory Investigation, 1954.

Tea: A symposium on the pharmacology and the physiologic and psychologic effects of tea. Edited by Henry J. Klaunberg, Ph.D., executive director, Biological Sciences Foundation, Limited. 8°, paper, 64 pp., with 6 illustrations and 6 tables. Washington, D. C.: Biological Sciences Foundation, Limited, 1955. $1.00.

Die cervikalen Vertebral-Syndrome: Eine vorläufige Bilanz der Kliniker. By R. Janzen et al. Edited by Prof. Dr. F. Reischauer, Essen. 8°, paper, 71 pp., with 5 illustrations. Stuttgart: Georg Thieme, 1955. DM 7.80.- $1.85. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Man's Ancestry: A primer of human phylogeny. By W. C. Osman Hill, M.D., F.F.R.S.E., prosector, Zoological Society of London. 8°, cloth, 194 pp., with 100 illustrations and 3 tables. Springfield, Illinois: Charles C Thomas, 1955. $4.25.

The Therapy of Skin Tuberculosis. By Gustav Riehl, M.D., professor of dermatology, University of Vienna, director, Lupus Institute of Vienna, and director, Department of Dermatology, Wilhelminen Hospital, Vienna; and Oswald Köpf, M.D., assistant, Department of Dermatology, Wilhelminen Hospital, Vienna. Translated and revised by Ernest A. Strakosch, M.D., Ph.D., director, Department of Dermatology, Presbyterian Hospital, Denver, Colorado. 8°, cloth, 247 pp., with 8 illustrations. Springfield, Illinois: Charles C Thomas, 1955. $6.75. (Publication No. 229, *American Lecture Series.*)

Clinical Endocrinology: For practitioners and students. By Laurence Martin, M.D. (Camb.), F.R.C.P. (Lond.), physician to Addnebrooke's Hospital, Cambridge, and assessor to the Regius Professor of Physic, University of Cambridge; and Martin Hynes, M.D. (Camb.), M.R.C.P. (Lond.), clinical pathologist to the Royal Northern Group of Hospitals. With a foreword by Sir Lionel Whitby, C.V.O., M.C., M.D., F.R.C.P., D.P.H., Regius Professor of Physic, University of Cambridge. Second edition. 8°, cloth, 253 pp., with 39 illustrations and 6 tables. Boston: Little, Brown and Company, 1954. $5.50.

Practical Medical Mycology. By Edmund L. Keeney, M.D. 8°, cloth, 145 pp., with 12 illustrations. Springfield, Illinois: Charles C Thomas, 1955. $4.50. (Publication No. 248, *American Lecture Series.*)

Forceps Deliveries. By Edward H. Dennen, M.D., professor of obstetrics and gynecology, director, Department of Obstetrics, and attending obstetrician, New York Polyclinic Medical School and Hospital, associate professor of clinical obstetrics and gynecology, Cornell University Medical College, attending obstetrician and gynecologist, New York Hospital, consulting obstetrician and gynecologist, Muhlenburg Hospital, Plainfield, New Jersey, and consulting obstetrician, Englewood Hospital, Englewood, New Jersey, United Hospital, Port Chester, New York, Mount Vernon Hospital, Mount Vernon, New York, and Greenwich Hospital, Greenwich, Connecticut. 8°, cloth, 228 pp., with 91 illustrations. Philadelphia: F. A. Davis Company, 1955. $6.50. (*Obstetrics and Gynecology,* edited by Claude E. Heaton, M.D.)

Grundfragen der Neurosenlehre: Aufbau und Sinn-Bild: Propädeutik einer medizinischen Psychologie. By Prof. Dr. J. H. Schultz, Berlin. 8°, cloth, 215 pp. Stuttgart: Georg Thieme, 1955. DM 24.- $5.70. (Distributed in the United States by the Intercontinental Book Corporation, New York City.)

Wiederherstellung des Harnweges und kunstliche Harnableitung bei Erkrankungen des Harnleiters: Indikationen und Methoden. By Prof. Dr. H. Boeminghaus, Düsseldorf. 8°, paper, 60 pp., with 53 illustrations. Stuttgart: Georg Thieme, 1955. DM 15.- $3.60. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Psychische Hygiene. By Prof. Dr. Ernst Brezina and Prof. Dr. Erwin Stransky. 8°, cloth, 282 pp. Vienna: Wilhelm Maudrich, 1955. $7.92. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

A Handbook of First Aid and Bandaging: Both an elementary and advanced course of training. By Arthur D. Belilios, M.B., B.S. (Lond.), D.P.H. (Eng.), lecturer, Wimbledon Technical College, examiner, General Nursing Council for England and Wales, divisional surgeon, S.J.A.B., and physician at the Wimbledon Hospital; Desmond K. Mulvany, M.S. (Lond.), F.R.C.S. (Eng.), F.R.C.P. (Irel.), surgeon, Hospital of St. John and St. Elizabeth, London, consulting surgeon, Wilson Hospital, Mitcham, Surrey, and divisional medical officer, B.R.C.S., Marylebone Division; and Katharine F. Armstrong, S.R.N., S.C.M., D.N. (Lond.). With a foreword by Sir Cecil P. G. Wakeley, Bt., K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., senior surgeon, King's College Hospital, director of surgical studies and lecturer in surgery, King's College Hospital Medical School, and consulting surgeon to the Royal Navy. Fourth edition. 16°, cloth, 463 pp., with 200 illustrations. London: Baillière, Tindall and Cox, 1955. $2.75. (Distributed by Williams and Wilkins, Baltimore.)

(Books Received continued on page xxvi)

NOTICES

CLOSED-CIRCUIT TELEVISION PROGRAM ON HEART DISEASE

The Tufts University School of Medicine and the New England Medical Center will present, "Grand Rounds," the second in a series of four national closed-circuit television programs, on Wednesday, February 15, at 9 p.m. The subject will be "The Cardiac Patient in Stress: Work, surgery, pregnancy." Doctors participating are C. Sidney Burwell, Benjamin Etsten, Samuel A. Levine, Samuel Proger, Merrill C. Sosman and Paul Dudley White.

The program may be viewed at the Somerset Hotel, Boston, and the Crown Hotel, Providence, Rhode Island.

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The House Officers' Association of the Boston City Hospital announces the schedule of the Tuesday evening lecture series to be held in the New Cheever Amphitheater, Dowling Building, Boston City Hospital, at 7 p.m., as follows:

February 14. Studies on the Growth Requirements and Metabolism of Normal and Malignant Human Cells in Tissue Culture. Dr. Harry Eagle, National Microbiological Institute, National Institutes of Health.

February 21. Metabolic Homeostasis in Patients with Nephritis and Nephrosis. Dr. Nathan B. Talbot, Harvard Medical School.

February 28. The Problem of Staphylococcal Infections Today. Dr. Walsh McDermott, Cornell University College of Medicine.

March 6. The Clinical Course of Lupus Erythematosus. Dr. A. McGehee, Johns Hopkins Hospital.

March 13. Mode of Action of the Mercurial Diuretics. Dr. Robert F. Pitts, Cornell University Medical College.

March 20. New Methods in Cardiac Surgery. Dr. Charles H. Hufnagel, Georgetown University School of Medicine.

March 27. Thyroid Tumors. Dr. Brown M. Dobyns, Western Reserve University School of Medicine.

April 3. Ulcerative Colitis. Dr. Leland S. McKittrick, Harvard Medical School.

SOUTH END MEDICAL CLUB

A meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, February 21, at 12 noon. Dr. Benedict F. Massell will speak on the subject "Problems of Rheumatic Fever and Rheumatic Heart Disease." All physicians are invited.

NEW ENGLAND RHEUMATISM SOCIETY

The winter meeting of the New England Rheumatism Society will be held in the Bigelow Amphitheater, Massachusetts General Hospital, Boston, on Friday, February 17, at 8 p.m.

The program is as follows:

Chemical and Immunological Studies of the Hemolytic Streptococcus and Its L-form. John T. Sharp, Willy Hijmans and Louis Dienes.

Experimental Production in the Rabbit of Autoimmune Bodies to Heart Tissue — Nature and Histologic Localization of the Reactive Antigen. Melvin H. Kaplan, Mary Meyserian and Audrey Swift.

Arthritis and Poliomyelitis. Leonard W. Cronkhite and Donald B. Martin.

Arteritis and Osteoarthropathy Associated with Frostbite. J. Peter Kulka and Joseph R. Blair.

Studies on the Metabolic Effects of Aspirin in Rheumatoid Arthritis. Daniel M. Bachman and Phoebe Krey.

YALE UNIVERSITY SCHOOL OF MEDICINE

A special conference on poliomyelitis will be held in connection with the annual Alumni Day program at the Yale University School of Medicine in Fitkin Amphitheater, on Wednesday, February 22, at 11 a.m.

The program is as follows:

Poliomyelitis: Recent advances in diagnosis. Dr. Dorothy M. Horstmann.

The Current Story in Vaccination. Dr. Francis L. Black and Dr. John R. Paul.

All physicians are invited.

MASSACHUSETTS TRUDEAU SOCIETY

A chest x-ray symposium of the Massachusetts Trudeau Society will be held in the amphitheater of the Peter Bent Brigham Hospital, Boston, Thursday, February 16, at 8 p.m. The program is as follows:

Acquired Nonvalvular Lesions. Dr. Merrill C. Sosman.
Acquired Valvular Lesions. Dr. G. B. Dealy, Jr.
Congenital Heart Lesions. Dr. Edward B. D. Neuhauser.
Correlation of Chest X-Ray Findings with Resected Specimens in Pulmonary Tuberculosis at a Boston Sanatorium. Dr. William Whitcomb.

Dr. Felix G. Fleischner will be moderator.
All physicians and medical students are invited.

AMERICAN COLLEGE OF CHEST PHYSICIANS AND OVERHOLT THORACIC CLINIC

A combined meeting of the New England States Chapter of the American College of Chest Physicians and the Overholt Thoracic Clinic will be held in the Joslin Auditorium, New England Deaconess Hospital, Boston, on Wednesday, February 15, at 4 p.m. Dr. Walter T. Goodale will talk on the subject "The Role of Pulmonary Vascular Disease in Atrial Septal Defect and Patent Ductus Arteriosus."

CONGRESSES ON BLOOD TRANSFUSION, BLOOD BANKS AND HEMATOLOGY

The Sixth Congress of the International Society of Blood Transfusion and the Sixth Congress of the International Society of Hematology will be held jointly and consecutively in Boston, Massachusetts, in August and September. In addition the American Association of Blood Banks will become a joint sponsor and hold its ninth annual meeting together with the International Transfusion Congress from September 3 through September 5. The Sixth International Hematology Congress will meet from August 27 through September 1. Joint programs are scheduled for September 1 and 3.

LOWELL INSTITUTE LECTURES ON MENTAL HEALTH

A series of free lectures on the subject "Mental Health in Colleges and Universities" is being given in the Dorothy Quincy Lecture Suite, John Hancock Building, 200 Berkeley Street, Boston, on Tuesdays, at 8 p.m. The final lecture will be on March 27. The lectures are given by Drs. Dana L. Farnsworth. Further information may be obtained from the Curator, Lowell Institute, Boston Public Library, Copley Square, Boston.

SOCIETY MEETINGS AND CONFERENCES

FEBRUARY 13. Harvard School of Public Health Forum. Page 241, issue of February 2.
FEBRUARY 13. New England Cardiovascular Society. Page 241, issue of February 2.
FEBRUARY 13–16. American College of Surgeons. Page 1136, issue of December 22.
FEBRUARY 14. Harvard Medical Society. Page 44, issue of January 5.
FEBRUARY 14, 21, 28, MARCH 6, 13, 20, 27 and APRIL 3. Boston City Hospital House Officers' Association. Page 297.
FEBRUARY 15. American College of Chest Physicians and Overholt Thoracic Clinic. Page 297.
FEBRUARY 15. Closed-Circuit Television Program on Heart Disease. Page 297.
FEBRUARY 16. Yale University School of Medicine. Page 242, issue of February 2.
FEBRUARY 16, MARCH 28 and APRIL 18. Greater Boston Medical Society. Page 208, issue of August 4.
FEBRUARY 16. Massachusetts Trudeau Society. Page 297.
FEBRUARY 17. New England Rheumatism Society. Page 297.
FEBRUARY 20–22. Atlanta Graduate Medical Assembly. Page 1136, issue of December 22.
FEBRUARY 20, MARCH 5, 19, APRIL 2 and 16. Hartford Medical Society. Page 242, issue of February 2.
FEBRUARY 21. South End Medical Club. Page 297.
FEBRUARY 22. Yale University School of Medicine. Page 297.
FEBRUARY 27. Benjamin Waterhouse Medical History Society. Page 241, issue of February 2.
FEBRUARY 29, MARCH 21 and APRIL 25. Massachusetts Heart Association. Page 623, issue of October 6.
MARCH 5 and APRIL 2. Fried Lecture Series. Page 535, issue of September 22.
MARCH 15–17. American Orthopsychiatric Association. Page 86, issue of January 12.
MARCH 19–22. American Academy of General Practice. Page 1092, issue of December 15.
MARCH 19–28 and JUNE 4–13. Army Medical Service Postgraduate Course. Page 84, issue of July 14.
MARCH 21 and APRIL 26. Phi Delta Epsilon Fraternity Graduate Club Program. Page 118, issue of July 21.
MARCH 24. Lowell Institute Lectures on Mental Health. Notice above.
MARCH 24 and 25. American Psychosomatic Society. Page 260, issue of August 11.
APRIL 3. Third Microcirculatory Conference. Page 139, issue of January 29.
APRIL 23–26. International Academy of Proctology. Page 86, issue of January 12.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 16

THURSDAY, FEBRUARY 16

Greater Boston Medical Society (dinner meeting). Doctor of the Year Award. Hotel Pensgate, 534 Beacon Street, Boston.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Yamins A, Beth Israel Hospital.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*11:15 a.m. Thoracic Conference. The Circuit Presents Cases of Medical and Surgical Interest. Drs. Harrison Black and Warren J. Taylor. Main Amphitheater, Peter Bent Brigham Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Staff Conference. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Tumor Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.

FRIDAY, FEBRUARY 17

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*1:00–3:00 p.m. Combined Medical-Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham, Saint Elizabeth's Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, FEBRUARY 18

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Benjamin Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*10:00 a.m. Combined Rounds. Second and Fourth (Harvard) Medical Services. Heart Station Conference Room, Boston City Hospital.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference (Blood Clinic). Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, FEBRUARY 20

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:00 m. Carney Lecture Series. Differential Diagnosis of Poliomyelitis. Dr. R. Cannon Eley. Archbishop Cushing Auditorium, Carney Hospital.
*12:00 m.–1:00 p.m. Pediatric Medical-Surgical Rounds. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Metabolism Conference. Dr. William Schwartz. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. X-Ray Conference. Dr. William Carey. Saint Elizabeth's Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Prevention of Neurological Sequelae of Spinal Anesthesia. Dr. Burnap. Surgical Conference Room, Peter Bent Brigham Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. Edward H. MacMahon. Stearns Auditorium, New England Center Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference of Greater Boston. (A) Regulation of Body Temperature and Changes in Anesthesia. (B) The Electroencephalogram and Stages of Anesthesia. Dr. Buskirk. Auditorium, Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

TUESDAY, FEBRUARY 21

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical Grand Rounds. Pathology Conference Room, Carney Hospital, Dorchester.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*10:30 a.m. Medical Grand Rounds. Dr. Walter Bauer. Main Conference Room (Ground Floor), Lemuel Shattuck Hospital.
*12:00 m.–1:00 p.m. Pediatric Grand Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic. (Cafeteria) New England Deaconess Hospital.
*2:00–3:00 p.m. Hematology Conference. Dr. Mario Stefanini. Saint Elizabeth's Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Benjamin Etsten. Stearns Auditorium, New England Center Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, FEBRUARY 22
Holiday

*Open to the medical profession.